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Specific Markers for Pancreatic Cancer

pancreatic cancer, to an in vitro method for the diagnosis of pancreatic cancer and/or the comprising at least one polypeptide identified by proteomics to be up-regulated in susceptibility to pancreatic cancer comprising the steps of a) obtaining a biological sample; and b) detecting and/or measuring the increase of specific markers as disclosed herein. Furthermore, screening methods relating to antagonists of the specific markers The present invention relates to markers for diagnosis of pancreatic cancer disclosed herein are provided.

with conventional imaging analyses. Most patients with pancreatic cancer present late in Among the causes for this late presentation is the lack of diagnostic methods for an patients with pancreatic cancer, accurate preoperative diagnosis is difficult to achieve earlier detection of the disease. Besides this lack of diagnostic methods, the high mortality Pancreatic cancer is a common cause of death in the Western world. It is one of the Therefore, the identification of new targets for early diagnosis of pancreatic tumors, and most aggressive malignant tumors, with an overall 5-year survival rate of 0.496. In many the course of the disease and have either locally extensive or metastatic disease. Overall, only up to 20% are candidates for resection and have the potential for curative surgery. of patients with pancreatic cancer is additionally caused by a lack of effective treatments. for the development of agents to treat pancreatic cancer is a challenge of paramount 2

for early diagnosis of the disease, and the long felt need for such markers, was overcome by the present invention by applying the new technology of proteomics. It was surprisingly found by using proteomic technology that a specific set of polypeptides are differentially expressed in pancreatic tissue obtained from individuals suffering from The problem of identifying polypeptides suitable as markers of pancreatic cancer HR/03.11.2003 23

used as markers for diagnosis of pencreatic cancer. The invention also provides an in vitro method for the diagnosis of pancreatic cancer comprising the steps of a) obtaining a biological sample; and b) detecting and/or measuring the increase of one or more polypepides as disclosed terein. Furthermore, screening methods relating to inhibitors and (54) Title: SPECIFIC MARKERS FOR PANCREATIC CANCER
(55) Abstract: The present invention provides polypepides which are up
to used as markers for diagnosis of pancreatic cancer. The invention also p
cancer and/or the susceptibility to pancreatic cancer comprising the steps
measuring the increase of one or more polypepides as disolosed herein.

provides polypeptides which are up- or down-regulated in pancreatic cancer and which can be

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Based on the polypeptides listed in tables 2 and 3, the present invention provides a marker for diagnosis of pancreatic cancer comprising at least one polypeptide selected from the group consisting of the polypeptides listed in tables 2 and/or 3 (Seq ID No. 1 to 24 and 26 to 49; and/or Seq ID No. 25 and 50 to 55). Thus, the term "marker" as used herein refers to one or more polypeptides that are regulated in cancer and that can be used to diagnose pancreatic cancer or a susceptibility to pancreatic cancer either alone or as combinations of multiple polypeptides that are known to be regulated in pancreatic cancer. Preferably, said polypeptides are selected from the group consisting of Seq. ID No. 25 and 50 to 54. More preferably, said polypeptides are selected from the group consisting of Seq ID No. 3, 4, 6, 9, 14, 15, 27, 31 to 35, 37, 39, 40; and/or Seq ID No. 50 to 52. Even more preferably, said polypeptides are selected from the group consisting of Seq ID No. 4, 6, 9, 14, 15, 31, 33 to 35 and/or Seq ID No. 51 and 52. Most preferably, said polypeptides are selected from the group consisting of Seq ID No. 4, 6, 9, 14, 15, 31, 33 to 35 and/or Seq ID No. 51 and 52. Most preferably, said polypeptides are selected from the group consisting of Seq ID No. 52.

The term "polypeptide" as used herein, refers to a polymer of amino acids, and not to a specific length. Thus, peptides, oligopeptides and proteins are included within the definition of polypeptide.

Preferably, the marker of this invention is a marker comprising at least one polypeptide selected from the group consisting of the polypeptides listed in table 2.

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19, 20, 23, 24, 27, 28, 31 to 40, 42 to 45, 47 and 48 from table 2 and/or Seq ID No. 25 and 50 to 54 from table 3. These polypeptides are induced at least two fold, as can be seen in of Seq ID No. 3, 4, 6, 9, 14, 15, 27, 31 to 35, 37, 39, 40 from table 2 and/or Seq ID No. 50 to 52 from table 3. These polypeptides are induced at least three fold, as can be seen in and 52 from table 3. These polypeptides are induced at least 4 fold, as can be seen in tables 2 and 3. Most preferably, said polypeptides are selected from the group consisting listed in tables 2 and/or 3, is used as a marker or as part of a marker for diagnosis of polypeptides are selected from the group consisting of Seq. ID No. 2 to 10, 12 to 15, 17, tables 2 and 3. More preferably, said polypeptides are selected from the group consisting tables 2 and 3. Even more preferably, said polypeptides are selected from the group consisting of Seq ID No. 4, 6, 9, 14, 15, 31, 33 to 35 from table 2 and/or Seq ID No. 51 of Seq ID No. 4, 6, 14, 15 and 31 from table 2 and/or Seq ID No. 52 from table 3, which urthermore, a polypeptide selected from the group consisting of the polypeptides pancreatic cancer and/or the susceptibility to pancreatic cancer. Preferably, said are the polypeptides that are induced five fold, as shown in tables 2 and 3. 2

The present invention pertains to a marker for diagnosis of pancreatic cancer comprising at least one polypeptide selected from the group consisting of the polypeptides listed in table 6. Preferably, said at least one polypeptide additionally does not include Seq ID No.s. 25 and 50 to 55.

In a preferred embodiment, the marker hereinbefore described additionally comprises at least one of the polypeptides listed in table 5.

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Several groups of polypeptides were identified as markers for pancreatic cancers:

One of the enzymes that caught our attention was Glutamine y-

glutamyltransferase/tissue transglutaminase (TGLC, Seq ID No. 54). It is a member of the transglutaminase family that catalyzes Ca2+ dependent reactions resulting in the post translational modification (cross-linking and conjugation with polyamines) of proteins at

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the level of glutamine and lysine residues (Greenberg, C. S., Birckbichler, P. J., and Rice, R. H. Transglutaminases: multifunctional cross-linking enzymes that stabilize tissues. FASEB J., 5: 3071-3077, 1991). Many different roles for this protein have been described, among them apoptosis, adhesion, and differentiation (Amendola, A., Pesus, L.,

- Piacentini, M., and Szondy, Z. "Tissue" transglutaminase in AIDS. J.Immunol.Methods, 265: 145-159, 2002). There is some controversy on the role of TGLC in apoptosis. While several pieces of evidence suggest that TGLC is a pro-apoptotic protein (Melino, G., et al., Mol.Cell Biol., 14: 6584-6596, 1994), Jason et al. found that TGLC acts in anti-apoptotic fashion (Boehm, J. E., et al. J.Biol.Chem, 277: 20127-20130, 2002). Many substrates of TGLC are major extra-cellular matrix (ECM) components such, as theorems.
 - 10 TGLC are major extra-cellular matrix (ECM) components such as fibronectin, osteonectin, and collagen, which makes TGLC an important enzyme in ECM development (Raghunath, M., et al., J.Clin.Invest, 98: 1174-1184, 1996., Nernes, Z., Jr., et al. J.Biol.Chem., 272: 20577-20583, 1997). Abnormal ECM development is involved in many pathological conditions such as fibrosis and may play a role in the proliferation of fibrous tissue observed in PC. Haroon et al. described that TGLC ECM-promoting abilities are an important part of the host response mechanism against tumor growth (Haroon, Z. A., et al., Lab Invest, 79: 1679-1686, 1999). Interestingly, loss of TGLC can be
 - abilities are an important part of the host response mechanism against tumor growth (Haroon, Z. A., et al., Lab Invest, 79: 1679-1686, 1999). Interestingly, loss of TGLC can be a biomarker for prostate adenocarcinoma (Birckbichler, P. J., et al., Cancer, 89: 412-423, 2000), which raises the question whether the measured TGLC is produced by neoplastic ductal cells and/or stromal cells. Measurements of mRNA levels in PC, normal tissue and PC cell lines indicate that TGLC is over expressed in both cell types (lacobuzio-Donahue, C. A., et al., Am.) Pathol., 166: 1239-1249, 2002), which would distinguish PC from prostate adenocarcinoma. Therefore, one preferred embodiment of the present invention is a marker comprising Seq ID No. 54.

Cytoskeletal proteins

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Several cytoskeletal proteins were detected at higher levels in PC than in surrounding tissue. One of these is gelsolin (Seq ID No. 3), a Ca²⁺ and PIP2 (polyphosphoinositide 4,5-bisphosphate) regulated severing and capping protein, which is a multifunctional actin regulatory protein and has roles in actin remodeling, motility, signaling, apoptosis and cancer (Maruta, H. G proteins cytoskeleton and cancer-Austin, Tex.: R.G. Landes, 1998). In several cancer studies, gelsolin expression has been described as down-regulated during carcinogenesis (breast, colon, stomach, bladder, prostate, and lung) (Asch, H. L., et al., Cancer Res., 56: 4841-4845, 1996; Dosaka-Akita, H., et al., Cancer Res., 58: 322-327, 1998, Prasad, S. C., et al. Electrophoresis, 18: 629-637, 1997). Another example for an up-regulated cytoskeletal protein is fascin (Seq ID No. 58), an

actin-bundling protein that has a role in cell matrix adhesion, cell interaction and migration. Fascin over expression has been reported in several cancers, such as breast, colon, and ovarian carcinoma (29). The present invention also features fascin 2 as a polypeptide up-regulated in pancreatic cancer (Seq ID No. 56). Thus, a preferred embodiment of the present invention is a marker comprising Seq ID. No. 3. In another preferred embodiment, the marker comprises Seq. ID No. 58. In another preferred embodiment, the marker comprises Seq. ID No. 58. In another preferred embodiment, the marker comprises Seq. ID No. 56.

In our study, cytokeratin 7 (Seq. ID No. 52) and cytokeratin 19 (Seq ID No. 33) showed strong expression in PC. Both have also been described in other cancers and have been linked with metastasis formation (Moll, R., Int.J.Biol.Markers, 9: 63-69, 1994.). High protein levels of actinin-4 (Seq ID No. 5) were detected in PC. This protein was linked by others with cell motility and cancer invasion (Honda, K., Yamada, T., Endo, R., Ino, Y., Gotoh, M., Tsuda, H., Yamada, Y., Chiba, H., and Hirohashi, S. J.Cell Biol., 140. 1383-1393, 1998.). Taken together, the apparent strong expression of cytoskeletal proteins is likely to be an important factor in the strong invasiveness and metastasisforming potential of PC. Thus, a preferred embodiment of the present invention is a marker comprising Seq ID. No. 52. In another preferred embodiment, the marker comprises Seq. 1D No. 33. In another preferred embodiment, the marker

20 Metastasis

Cancer of exocrine pancreas is characterized by extensive local invasion, early lymphatic and hematogenous metastasis. Metastasis in PC has been found in the skeleton, eye, bladder, etc. The extent of angiogenesis depends on the balance between pro-angiogenic or anti-angiogenic factors released from cancer and host cell. Currently, intratumoral microvessel density (IMD) measured by immunocytochemistry appears to be the most reliable parameter for assessing angiogenic activity. Patients with high IMD have decreased survival rates in a variety of cancers (Fujioka, S., et al., Cancer, 92: 1788-1797, 2001). Thymidine phosphorylase (TYPH or TP, Seq ID No. 31) which is identical to platelet-derived endothelial cell growth factor, is strongly expressed in PC and stimulates the chemotaxis of endothelial cells through the 2-deoxy-D-tibose, degradation products of thymidine by TP, thus indirectly inducing angiogenesis (Haraguchi, M., et al. Nature, 368: 198, 1994.). Shuichi Fujioka et al. found that IMD and TP status were independent predictive indicators for overall as well as relapse-free survival in PC (Fujioka, S., et al., Cancer, 92: 1788-1797, 2001). An additional protein detected at higher levels in PC than in surrounding tissue likely involved in metastasis formation is

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osteoblast specific factor 2 (Seq ID No.53), a putative bone adhesion protein. Breast carcinoma commonly metastasizes to bone (Guise, T. A. Cancer, 88: 2892-2898, 2000). Although the role of this protein in PC is not clearly established, our findings suggest a similar role for osteoblast specific factor 2 in PC. Thus, a preferred embodiment of the present invention is a marker comprising Seq ID. No. 31. In another preferred embodiment, the marker comprises Seq. ID No. 53.

Small GTP-binding proteins

Four small GTP-binding proteins and interacting proteins were more strongly expressed in PC than in normal pancreas tissue. These include RAN (Seq. ID No. 27), GBLP (guanine nucleotide binding protein β subunit-like protein RACK1, Seq. ID No. 47), GDIR (Rho GDP dissociation inhibitor 1, Seq. ID No. 55), and IQG1 or IQGAP1 (Ras gipase activating like protein, Seq ID No. 25). Small GTP-binding proteins constitute a superfamily, which is structurally classified into at least five families: the Ras, Rho Rah, Sar1 Arf and Ran families and are involved in the remistion of cases.

Rho, Rab, Sar1/Arf, and Ran families and are involved in the regulation of gene expression, cytoskeletal reorganization, and nucleocytoplasmic transport (Takai, Y., et al. Physiol Rev., 81: 153-208, 2001). RAN is known to enhance androgen receptor-mediated transactivation and was shown to be overexpressed in prostate cancer (Sampson, E. R., et al., J. Biol.Regul.Homeost.Agents, 15: 123-129, 2001). Increased expression of RAN in 81% of prostate tumor cases, may contribute to over proliferation of prostate tumor cells (Li, P., et al., Am J Pathol., 161: 1467-1474,2002). GBLP is an anchoring protein for

angiogenically active tissue (Berns, H., et al., FASEB J., 14: 2549-2558, 2000). Further more, mRNA expression of GBLP is detected in epithelial cells of human colon carcinoma and proliferating epithelial cell of normal colon tissue. Therefore, there is a likely link between high GBLP expression and tumor growth. GDIR (Rho GDP dissociation inhibitor) had been found up-regulated in a chemoresistant fibrosarcoma

important role in angiogenesis and cancer growth. Berns et al. found GBLP up-regulated

in during angiogenesis in vitro and also associated with nonendothelial cells in

activated protein kinase CB and a variety of other proteins. Protein kinase C plays an

cell line by 2D-PAGE (Sinha, P., et al., Electrophoresis, 20: 2961-2969, 1999) and may block apoptotic signal pathway mediated by Ras and c-jun kinase, resulting in the increase resistance against environmental stress. IQGI (Ras GTPase-activating-like protein) is a widely expressed 190-kDa Cdc42-, Rac1-, and calmodulin-binding protein that interacts with F-actin in vivo and that can cross-link F-actin microfilaments in vitro. IQGI negatively regulates the Ecc-based (E-cadherin/catenin complex) cell-cell adhesion by dissociating alpha-catenin. Up-regulation of IQGAP1 is correlated with the malignant

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phenotype in gastric cancer (Sugimoto, N., et al., J. Hum. Genet., 46: 21-25, 2001). By immunohistochemical analysis, IQGAP1 was found overexpressed in colorectal cardnoma and associated with carcinoma invasion (Nabeshima, K., et al., Cancer Lett., 176: 101-109, 2002). Since cancer invasiveness is associated with the localized disruption of cell-cell adhesion, both our results and Iacobuzio-Donahue et al.'s data suggest that IQGAP1 may be involved in the disruption of local adhesion and in PC invasion to surrounding tissue. Thus, a preferred embodiment of the present invention is a marker comprising Seq ID No. 27. In another preferred embodiment, the marker comprises Seq.

S100 protein family

ID No. 47. In another preferred embodiment, the marker comprises Seq. ID No. 55. In

another preferred embodiment, the marker comprises Seq. ID No. 25.

mucosa, as shown by proteomica analysis (Stulik, J., et al., Electrophoresis, 20: 1047-1054, Frends Biochem.Sci., 21: 134-140, 1996). S100A8 and S100A9 are negatively regulated by earcinogenesis (Gebhardt, C., et al., Oncogene, 21: 4266-4276, 2002). These proteins are 1999). S100A9 has been detected in cultured human adenocarcinoma (AC) cells derived diseases) (Donato, R. Int.J.Biochem.Cell Biol., 33: 637-668, 2001). S100A8 and S100A9 adenocarcinoma (Arai, K., et al., Oncol.Rep., 8: 591-596, 2001). Iacobuzio-Donahue et cheumatoid arthritis, cystic fibrosis, psoriasis, allergic dermatitis, inflammatory bowel also more strongly expressed in colorectal carcinoma than in matched normal colon endothelial origin and accumulation at sites of acute and chronic inflammation (e.g. intracellular as well as extracellular functions (Schafer, B. W. and Heizmann, C. W. glucocorticoids in a c-Fos-dependent manner and over expressed throughout skin Another protein with high-level expression in PC is \$109 (\$100A9, MRP-14, an form a noncovalent heterodimer protein complex called calprotectin. Current from various organs, and is associated with tumor differentiation in pulmonary al's work indicates that over expression of S100A4 in PC is associated with poor characterized by cell type-specific expression in cells of epithelial, myeloid and homologous low molecular weight calcium binding proteins. Calgranulins are reports support that both of \$100A9 and \$100 A8 have wide range of possible calgranulin B, Seq ID No. 49), a member of the S100 protein family of highly 2

Annexin

2002). Thus, a preferred embodiment of the present invention is a marker comprising

differentiation and DNA hypomethylation (Rosty, C., et al., Am.J.Pathol., 160. 45-50,

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or an indirect link with PC, e.g. BGH3 (TGF- $\beta 1$ -induced protein, Seq ID No. 6) which is a secretory protein and acts as a marker for biologically active TGF- β 1 (Langham, R. G., Some additional proteins highly expressed in PC may have either clear roles in PC et al., Transplantation, 72: 1826-1829, 2001). Thus, a preferred embodiment of the present invention is a marker comprising Seq ID No. 6.

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invention provides an in vitro method for the diagnosis of pancreatic cancer and/or the susceptibility to pancreatic cancer comprising the steps of obtaining a biological sample; and detecting and/or measuring the increase of a marker described hereinbefore. The term "detection" as used herein refers to the qualitative determination of the absence or presence of polypeptides. The term "measured" as used herein refers to the quantitative determination of the differences in expression of polypeptides in biological samples from Antibodies recognizing the polypeptides listed in table 2, 3, 5 and/or 6 can either be generated for the purpose of detecting said polypeptides, eg. by immunizing rabbits with With the identification of polypeptides regulated in pancreatic cancer, the present patients with pancreatic cancer and biological samples from healthy individuals. Methods for detection and/or measurement of polypeptides in biological samples are well known purified proteins, or known antibodies recognizing said polypeptides can be used. For example, an antibody capable of binding to the denatured proteins, such as a polyclonal antibody, can be used to detect the peptides of this invention in a Western Blot. An example for a method to measure a marker is an ELISA. This type of protein quantitation diagnostic marker for pancreatic cancer is by analysing biopsy specimens for the presence or absence of the markers of this invention. Methods for the detection of these markers are well known in the art and include, but are not limited to, immunohistochemistry or immunofluorescent detection of the presence or absence of the polypeptides of the mentioned hereinbefore are described in Harlow, E. and Lane, D. Antibodies: A is based on an antibody capable of capturing a specifc antigen, and a second antibody capable of detecting the captured antigen. A further method for the detection of a marker of this invention. Methods for preparation and use of antibodies, and the assays in the art and include, but are not limited to, Western-blotting, ELISAs or RIAs Laboratory Manual, (1988), Cold Spring Harbor Laboratory Press.

The accuracy of the diagnosis of pancreatic cancer can be increased by analysing combinations of multiple polypeptides listed in tables table 2, 3, 5 and/or 6. Thus, the in vitro method herein before described, comprises a marker which comprises at least two, preferably at least three, more preferably at least four, even more preferably at least five, and most preferably at least six of the polypeptides listed in table 2,3, 5 and/or 6. For diagnosis of pancreatic cancer, suitable biological samples need to be analysed for the presence or absence of a marker. Said biological samples can be serum, plasma,

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pancreatic juice or cells of pancreatic tissue. Cells from pancreatic tissue can be obtained by ERCP, secretin stimulation, fine-needle aspiration, cytologic brushings and large-bore needle biopsy.

It is also possible to diagnose pancreatic cancer by detecting and/or measuring nucleic acid molecules coding for the marker hereinbefore described. Preferably, said nucleic acid molecule is RNA or DNA. In another embodiment, said DNA is a cDNA.

In one embodiment of the present invention, the in vitro method herein before described comprises comparing the expression levels of at least two of the nucleic acids encoding said polypeptides in an individual suspected to suffer from pancreatic cancer and/or to be susceptible to pancreatic cancer, to the expression levels of the same nucleic acids in a healthy individual.

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In another embodiment of the present invention the in vitro method herein before described comprises comparing the expression level of said marker in an individual suspected to suffer from pancreatic cancer and/or to be susceptible to pancreatic cancer to the expression levels of the same marker in a healthy individual. In a more preferred embodiment of the in vitro method, an increase or decrease of the expression levels of said marker is indicative of pancreatic cancer or the susceptibility to pancreatic cancer.

The present invention also provides a screening method for identifying and/or obtaining a compound which interacts with a polypeptide listed in table 2 and/or 3 whose expression is upregulated in pancreatic cancer, comprising the steps of contacting 25 said polypeptide with a compound or a plurality of compounds under conditions which allow interaction of said compound with said polypeptide, and detecting the interaction between said compound or plurality of compounds with said polypeptide.

The "interaction" in the screening methods as disclosed herein may be measured by conventional methods. The type of conventional method for testing the interaction of a

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compound with a polypeptide that is soluble, as opposed to membrane associated, can be an in vitro method using either purified recombinant polypeptide, or native polypeptide purified from cells that endogenously express the polypeptide. As a non-limiting example, a polypeptide of the invention can be bound to beads or immobilized on plastic or other surfaces, and interaction of a compound with the polypeptide can be measured

or other surfaces, and interaction of a compound with the polypeptide can be measured by either using a labelled compound and measuring the label bound to the polypeptide or by displacement of a labeled known ligand from said polypeptide. For polypeptides that are associated with the cell membrane on the cell surface, or which are expressed as transmembrane or integral membrane polypeptides, the interaction of a compound with said polypeptides can be detected with different methods which include, but are not limited to, methods using cells that either normally express the polypeptide or in which the polypeptide is overexpressed, eg. by detecting displacement of a known ligand which is labeled by the compound to be screened.

with such a polypeptide

Interaction assays to be employed in the method disclosed herein may comprise FRET-assays (fluorescence resonance energy transfer; as described, inter alia, in Ng. Science 283 (1999), 2085-2089 or Ubarretxena-Belandia, Biochem. 38 (1999), 7398-7405), TR-FRETs and biochemical assays as disclosed herein. Furthermore, commercial assays like "Amplified Luminescent Proximity Homogenous AssayTM" (BioSignal Packard) may be employed. Further methods are well known in the art and, inter alia, described in Fernandez, Curr. Opin. Chem. Biol. 2 (1998), 547-603.

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The "test for interaction" may also be carried out by specific immunological and/or biochemical assays which are well known in the art and which comprise, e.g., homogenous and heterogenous assays as described herein below. Said interaction assays employing read-out systems are well known in the art and comprise, inter alia, two-09/02911; and as exemplified in the appended examples), GST-pull-down columns, copecipitation assays from cell extracts as described, inter alia, in Kasus-Jacobi, Oncogene 19 (2000), 2052-2059, "Interaction-trap" systems (as described, inter alia, in US

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6,004,746) expression cloning (e.g. lamda gt11), phage display (as described, inter alia, in US 5,541,109), in vitro binding assays and the like. Further interaction assay methods and corresponding read out systems are, inter alia, described in US 5,525,490, WO 99/51741, WO 00/17221, WO 00/14271 or WO 00/05410. Vidal and Legrain (1999) in Nucleic Acids Research 27, 919-929 describe, review and summarize further interaction assays known in the art which may be employed in accordance with the present invention.

Homogeneous (interaction) assays comprise assays wherein the binding partners remain in solution and comprise assays, like agglutination assays. Heterogeneous assays comprise assays like, inter alia, immuno assays, for example, Enzyme Linked Immunosorbent Assays (ELISA), Radioactive Immunoassays (RIA), Immuno Radiometric Assays (IRMA), Flow Injection Analysis (FIA), Flow Activated Cell Sorting (FACS), Chemiluminescent Immuno Assays (CLIA) or Electrogenerated Chemiluminescent (ECL) reporting.

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has not been contacted with said compound; and d) quantitatively relating the activity as to (c) is indicative for an inhibitor or antagonist. The terms inhibitors and antagonists as host may therefore be genetically modified with a nucleic acid molecule encoding such a obtaining a compound which is an inhibitor or an antagonist of a polypeptide listed in able 2 and/or 3 whose expression is upregulated in pancreatic cancer, comprising the steps of a) contacting said polypeptide with a compound identified and/or obtained by compound with said polypeptide; b) determining the activity of said polypeptide; c) determining the activity of said polypeptide expressed in the host as defined in (a), which determined in (b) and (c), wherein a decreased activity determined in (b) in comparison used herein are used interchangeably. This screening assay can be performed either as an in vitro assay, or as a host-based assay. The host to be employed in the screening methods of the present invention and comprising and/or expressing a polypeptide listed in table 2, 3, 5 and/or 6 may comprise prokaryotic as well as eukaryotic cells. Said cells may comprise bacterial cells, yeast cells, as well as cultured (tissue) cell lines, inter alia, derived from mammals. Furthermore animals may also be employed as hosts, for example an non-human transgenic animal. Accordingly, said host (cell) may be transfected or transformed with the vector comprising a nucleic acid molecule coding for a polypeptide which is differentially regulated in pancreatic cancer as disclosed herein. Said host cell or the screening method described above under conditions which allow interaction of said The present invention further provides a screening method for identifying and/or 20 25 33

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polypeptide or with a vector comprising such a nucleic acid molecule. The term "genetically modified" means that the host cell or host comprises in addition to its natural genome a nucleic acid molecule or vector coding for a polypeptide listed in table 2, 3, 5 and/or 6 or at least a fragment therof. Said additional genetic material may be introduced into the host (cell) or into one of its predecessors/parents. The nucleic acid molecule or vector may be present in the genetically modified host cell or host either as an independent molecule outside the genome, preferably as a molecule which is capable of replication, or it may be stably integrated into the genome of the host cell or host.

As mentioned herein above, the host cell of the present invention may be any prokaryotic or eukaryotic cell. Suitable prokaryotic cells are those generally used for doning like E. coli or Bacillus subtilis. Yet, these prokaryotic host cells are also envisaged in the screening methods disclosed herein. Furthermore, eukaryotic cells compries, for example, fungal or animal cells. Examples for suitable fungal cells are yeast cells, preferably those of the genus Saccharomyces and most preferably those of the species Saccharomyces cerevisiae. Suitable animal cells are, for instance, insect cells, vertebrate cells, preferably mammalian cells, such as e.g. CHO, HeLa, NIH3T3 or MOLT-4. Further suitable cell lines known in the art are obtainable from cell line depositories, like the American Type Culture Collection (ATCC).

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The hosts may also be selected from non-human mammals, most preferably mice, rats, sheep, calves, dogs, monkeys or apes. As described herein above, said animals/mammals also comprise non-human transgenic animals, which preferably express at least one polypeptide differentially regulated in pancreatic cancer as disclosed herein. Preferably, said polypeptide is a polypeptide which is up-regulated in tissue derived from patients with pancreatic cancer. Yet it is also envisaged that non-human present invention or alternatively, which comprise silenced or less efficient versions of transgenic animals be produced which do not express marker genes as disclosed herein or who express limited amounts of said marker gene products. Said animals are preferably human animals comprising and/or expressing the up-regulated polypeptides of the down-regulated polypeptides are useful models for studying the development of pancreatic cancer and provide for useful models for testing drugs and therapeutics for related to polypeptides which are down-regulated in pancreatic cancer. Transgenic nonpancreatic cancer treatment and/or prevention. 22 8

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A compound which interacts with a polypeptide listed in table 2, 3, 5 and/or 6 and which inhibits or antagonizes said polypeptide is identified by determining the activity of said polypeptide in the presence of said compound.

- The term "activity" as used herein relates to the functional property or properties of a specific polypeptide. For the enzymes listed in table 2, 3, 5 and/or 6, the term "activity" relates to the enzymatic activity of a specific polypeptide. Activity assays for the enzymes listed in table 2, 3, 5 and/or 6 are well known.
- 10 For adhesion molecules listed in table 2, 3, 5 and/or 6, the term "activity" relates to the adhesive properties of a polypeptide and may determined using assays such as, but not limited to, adhesion assays, cell spreading assays, or in vitro interaction of the adhesion molecule with a known ligand. Such assays are well known in the art.
- For cytoskeletal proteins, the term "activity" relates to the regulation of the cytoskeleton by such polypeptides, or to their incorporation into the cytoskeleton. As a non-limiting example, the ability of Gelsolin to regulate actin polymerization, or of Filamin A to promote orthogonal branching of actin filaments, may be determined using in vitro actin polymerization assays. Activity in relation to the regulation of cytoskeletal structures may further be determined by, as non-limiting examples, cell spreading assays, cell migration assays, cell proliferation assays or immunofluorecence assays, or by staining actin filaments with fluorescently labeled phalloidin. All of these assays are well known to the person skilled in the art.
- For ion channels (Chloride intracellular channel protein) the term "activity" relates to ion flux (Chloride lux) across the membrane. Methods to determine ion flux across membranes are well known to the person skilled in the art.

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For transcription factors, eg. KIAA 1034, the term "activity" relates to their ability to regulate gene transcription. The transcriptional activity of a polypeptide can be determined using commonly used assays, such as a reporter gene assay.

For growth factors and hormones or their receptors, the term "activity" relates to their ablity to bind to their receptors or ligands, respectively, and to induce receptor activation and subsequent signaling cascades, and/or it relates to the factor's or receptor's ability to mediate the cellular function or functions eventually caused by growth factor or hormone binding to receptors can be determined by commonly known ligand binding assays. Receptor activation can be determined by testing for receptor auto-phosphorylation, or by assaying for modification or recruitment of downstream signaling mediators to the receptors (by immunoprecipitation and Western Blotting of signaling complexes). Cellular functions regulated by growth factors or hormones and their receptors can be cell proliferation (eg determined by using thymidine incorporation or cell counts), cell migration assays (eg determined by using DAPI staining), angiogenesis assays (eg in vitro assays to measure endothelial tube formation that are commercially available). In addition to these assays, other assays may be used as well to determine these and other cellular functions.

Inhibitors or antagonists of a polypeptide listed in tables 2 and/or 3 are identified by the screening method described above when there is a decreased activity determined in the presence of the compound in comparison to the absence of the compound in the screening method, which is indicative for an inhibitor or antagonist.

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Further to the screening methods disclosed above, this invention provides a screening method for identifying and/or obtaining a compound which is an inhibitor of the expression of a polypeptide listed in tables 2 and/or 3 whose expression is upregulated in pancreatic cancer, comprising the steps of a) contacting a host which expresses said polypeptide with a compound; b) determining the expression level and/or activity of said polypeptide; c) determining the expression level and/or activity of said polypeptide in the host as defined in (a), which has not been contacted with said compound; and d) quantitatively relating the expression level of said polypeptide as determined in (b) and

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(c), wherein a decreased expression level determined in (b) in comparison to (c) is indicative for an inhibitor of the expression of said polypeptide.

An inhibitor of the expression of a polypeptide listed in table 2, 3, 5 and/or 6 is identified by the screening method described hereinbefore when a decreased expression of the protein is determined in the presence of the compound in comparison to the absence of the compound in the screening method, which is indicative for an inhibitor of expression of a polypeptide.

listed table 2, 3, 5 and/or 6 which is up-regulated in pancreatic cancer, in cells, preferably in a pancreatic adenocarcinoma cell line, which are elevated as compared to the expression levels of the same polypeptide in healthy pancreatic cells. Preferably, expression levels are at least 2 fold, more preferably at least 3 fold, even more preferably at least 4 fold, most preferably at least 5 fold higher than in healthy pancreatic cells.

Furthermore, the present invention provides a compound identified and/or obtained by any of the screening methods hereinbefore described. Said compound is further comprised in a pharmaceutical composition. A method for the preparation of said pharmaceutical composition comprising formulating said compound in a pharmaceutically acceptable carrier or diluent is also claimed. Any conventional carrier material can be utilized. The carrier material can be an organic or inorganic one suitable for eteral, percutaneous or parenterial administration. Suitable carriers include water, gelatin, gum arabic, lactose, starch, magnesium stearate, talc, vegetable oils, polyalkyleneglycols, petroleum jelly and the like. Furthermore, the pharmaceutical preparations may contain other pharmaceutically active agents. Additional additives such as flavoring agents, stabilizers, emulsifying agents, buffers and the like may be added in accordance with accepted practices of pharmaceutical compounding.

Said compound may be used for the preparation of a medicament for the treatment or prevention of pancreatic cancer. In addition, said compound may also be used for the preparation of a diagnostic composition for diagnosing pancreatic cancer or a predisposition for pancreatic cancer. Preferably, said compound comprises an antibody, an antibody-derivative, an antibody fragment, a peptide or an antisense construct.

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Within the scope of the present invention, antibodies against the proteins listed in tables 2 and/or 3, or antigen-binding fragments thereof, may be used in an in vitro method for the diagnosis of pancreatic cancer.

provides a kit for the diagnosis of pancreatic cancer comprising one or more of the antibodies, or antigen-binding fragments thereof, described above. Another kit provided by this invention is a kit for the diagnosis of pancreatic cancer comprising one or more of the nucleic acids coding for the marker hereinbefore described. Yet another kit provided to by this invention is a kit for screening of compounds that antagonize any of the polypeptides listed in tables 2 and/or 3 or inhibit the expression of any of said polypeptides.

The present invention pertains to a marker for diagnosis of pancreatic cancer comprising at least one polypeptide selected from the group consisting of the polypeptides listed in table 6. Preferably, said marker does not include Seq ID No.s 25 and 50 to 55. In a more preferred embodiment, said marker comprises at least one of the polypeptides listed in table 5.

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The present invention also provides an in vitro method for the diagnosis of pancreatic cancer and/or the susceptibility to pancreatic cancer comprising the steps of

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a) obtaining a biological sample; and

 b) detecting and/or measuring the increase of at least one of the polypeptides listed in table 6. Preferably, said in vitro method additionally comprises the step of detecting and/or measuring the decrease of at least one of the polypeptides listed in table 5. More preferably, in said vitro method, said at least one polypeptide does not include Seq ID No.s 25 and 50 to 55. Even more preferably, in said vitro method, said biological sample is derived from the group consisting of serum, plasma, pancreatic juice and cells of pancreatic tissue.

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The present invention further provides an in vitro method for the diagnosis of pancreatic cancer and/or the susceptibility to pancreatic cancer comprising the steps of

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a) obtaining a biological sample; and

 b) detecting and/or measuring the increase of at least one nucleic acid coding for the marker hereinbefore described. Preferably, in said in vitro method, said nucleic acid molecule is RNA or DNA. More preferably, in said in vitro method, said DNA is a cDNA.

In a further more preferred embodiment of any of the in vitro methods hereinbefore described, the expression levels of at least one of said nucleic acids in an individual suspected to suffer from pancreatic cancer and/or to be susceptible to pancreatic cancer is compared to the expression levels of the same nucleic acids in a healthy individual. In a most preferred embodiment of any of the in vitro methods hereinbefore described, the expression level of said marker in an individual suspected to suffer from pancreatic cancer and/or to be susceptible to pancreatic cancer is compared to the expression levels of the same marker in a healthy individual.

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In a further preferred embodiment of the in vitro method hereinbefore described,

an increase of the expression levels of said marker is indicative of pancreatic cancer or the

susceptibility to pancreatic cancer.

The present invention also pertains to a screening method for identifying and/or obtaining a compound which interacts with a polypeptide selected from the group consisting of the polypeptides listed in table 6 whose expression is upregulated in pancreatic cancer, comprising the steps of

- a) contacting said polypeptide with a compound or a plurality of compounds under conditions which allow interaction of said compound with said polypeptide; and
- b) detecting the interaction between said compound or plurality of compounds with said polypeptide.

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Furthermore, the present invention provides a screening method for identifying and/or obtaining a compound which is an inhibitor or an antagonist of a polypeptide listed in table 6 whose expression is upregulated in pancreatic cancer, comprising the steps of

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contacting said polypeptide with a compound identified and/or obtained by the screening method of claim 39 under conditions which allow interaction of said compound with said polypeptide;

b) determining the activity of said polypeptide;

c) determining the activity of said polypeptide expressed in the host as defined in
 (a), which has not been contacted with said compound; and

d) quantitatively relating the activity as determined in (b) and (c), wherein a decreased activity determined in (b) in comparison to (c) is indicative for an inhibitor or antagonist.

The present invention also provides a screening method for identifying and/or obtaining a compound which is an inhibitor of the expression of a polypeptide selected from the group consisting of the polypeptides listed in table 6 whose expression is upregulated in pancreatic cancer, comprising the steps of

a) contacting a host which expresses said polypeptide with a compound,

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b) determining the expression level and/or activity of said polypeptide;

c) determining the expression level and/or activity of said polypeptide in the host as defined in (a), which has not been contacted with said compound; and

 d) quantitatively relating the expression level of said polypeptide as determined in (b) and (c), wherein a decreased expression level determined in (b) in comparison to (c) is indicative for an inhibitor of the expression of said polypeptide.

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The present invention provides a compound identified and/or obtained by the screening methods hereinbefore described.

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In addition, the present invention provides a pharmaceutical composition comprising the compound hereinbefore described. Also provided is a method for the preparation of the pharmaceutical composition hereinbefore described comprising to formulating the compound hereinbefore described in a pharmaceutically acceptable carrier or dilutent.

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The present invention provides a use of a compound hereinbefore described for the preparation of a medicament for the treatment or prevention of pancreatic cancer. Also provided is a use of a compound hereinbefore described for the preparation of a diagnostic composition for diagnosting pancreatic cancer or a predisposition for pancreatic cancer. In a preferred embodiment, the uses hereinbefore described relate to a compound comprising an antibody, an antibody-derivative, an antibody fragment, a peptide or an antisense construct.

Within the scope of the present invention, antibodies against the proteins
10 listed in tables 5 and/or 6, or antigen-binding fragments thereof, may be used in an in vitro method for the diagnosis of pancreatic cancer.

In order to efficiently perform diagnostic screenings, the present invention provides a kit for the diagnosis of pancreatic cancer comprising one or more of the antibodies, or antigen-binding fragments thereof, described above. Another kit provided by this invention is a kit for the diagnosis of pancreatic cancer comprising one or more of the nucleic acids coding for the marker hereinbefore described. Yet another kit provided by this invention is a kit for screening of compounds that antagonize any of the polypeptides listed in tables 5 and/or 6 or inhibit the expression of any of said polypeptides.

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In the present invention, the proteins, compounds, kits, methods and uses substantially as herein before described, especially with reference to the foregoing examples are also claimed.

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Examples:

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Collection of tissue samples

Pancreatic carcinomas and adjacent tissue were collected from the patients listed in

Samples were collected shortly after the resection (less than 30 minutes), and fast frozen in liquid nitrogen for about 1 minute, then stored in a freezer at a temperature of -80°C.

10 Characterization of formalin-fixed specimens

Histopathological characterization was carried out by using hematoxylin-eosin-stained sections of formalin-fixed and paraffin-embedded specimens. Tumors were classified using the WHO system. The types of pancreatic carcinomas included in the study are shown in table 1.

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The twelve pancreatic carcinoma samples used in this study were ductal carcinomas which constitute the overwhelming proportion of pancreatic carcinomas. The patient-matched samples from histologically normal tissue surrounding the carcinoma were used as controls. We carried out 12 pairs of 2-dimensional electrophoresis maps for

- comparing protein expression between tumor tissue and normal control tissue. For protein identification, the samples were pooled, thus generating pan-Carcinoma and pan-Normal protein extracts. Quantification was carried out in two steps: (I) Gels from the pooled samples were compared using the PDQuest image analysis software. (II) The changes identified at the level of the pooled samples were cross-validated by an analysis of the individual samples. The change factors shown in table 2, 3, 5 and 6 were determined
 - the manyidual samples.

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Preparation of samples for electrophoresis

Samples cleaned of clots and contaminating tissue were frozen in liquid nitrogen, then ground to powder. Samples were suspended in lysis buffer (8M urea, 4% CHAPS, 40mMol/L Tris-Cl, 0.5% carier amphollytes, 100mMol/L DTT and 0.1ig/il PMSF) and centrifuged at 12000rpm for 30 minutes. The supernatants were stored at -80°C. The protein concentration in the extracts was determined by the Bradford method (Bradford, M. Anal. Biochem. 72, 248 (1976).

Two-dimensional gel electrophoresis

Samples containing 1 mg of protein were loaded onto the rehydrated IPG strip (18 cm, pH3~10) by using the cup loading method. IEF was performed using Pharmacia Multiphor apparatuses under the following conditions: First, the voltage was increased 200V-5000V over 24hrs, then a constant voltage of 5000V was applied for 24 hrs, the running temperature was 20°C. After IEF, the strips were equilibrated with 10 ml equilibration solution I (6 M Urea, 50 mM Tris pH 8.8, 30 % Glycerol, 2.0 % SDS, 30 mM Dithioerythritol) for 15 min, then for another 15 min with equilibration solution II (6 M Urea, 50 mM Tris pH 8.8, 30 % Glycerol, 2.0 % SDS, 0.23 M Iodoacetamide).

The second dimension SDS polyacrylamide gel electrophoresis (SDS-PAGE) was
carried out using a Hoefer ISO_DALT apparatus (10 gels/run, 24×20 cm), IEF strips were
loaded onto 12% homogeneous polyacrylamide gels (1.5 mm x 24 cm × 20 cm). The gels
were run in TGS_Buffer (250 mM Tris, 1.92 M Glycine, 1% (w/v) SDS, pH = 8.3, BioRad) at a constant voltage (80 V, 20°C).

25 Gel fixation and staining

Gels were fixed in 50% Methanol/20% acetic acid for 30 min, then washed in ultrapure water for 30 min and stained with NOVEX Colloidal Blue staining Kit (Invitrogen) following the manufacturer's recommendations.

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Protein Identification

The protein identification was performed using a two-step procedure.

In-gel digestion

Spots were picked and transferred into 96-well by a spot picking robot. From each gel, 600-800 spots were picked. The spots were destained with 100µl of 30% acentonitrile in 50Mm ammonium bicarbonate, washed in ultra pure-water and dried in a speed vac evaporator. The dry gel pieces were digested with 10ng/µl trypsin (Promega, Madison, USA) solution in 500 nM ammonium bicarbonate at room temperature for 16 h maximum. The peptides from each spot were extracted with 20µl of 0.19% trifluore acetic acid (TFA) in 50% acetonitrile. The matrix solution consisted of 0.025%(w/v) alfacyano-4-hydroxy cinammic acid (Sigma) in 50% acetonitrile(0.1% TFA with internal standard peptides des-Arg-Bradykinin(Sigma, MW 904.4681 Da) and adrenocorticotropic hormone fragment 18-39 (Sigma, MW 2465.1989 Da).

Analysis by MALDI-TOF

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1.5ul of peptide extract and 1.0µl of matrix solution were stimulaneously applied to the spots on the MS target. Recrytallization was carried out as specified by the instruments manufacturer. The samples were analyzed in a MALDI-time of flight Mass spectrometer (Autoflex, Bruker Analytics, Bremen, Germany). Peak annotation and database search by peptide matching was performed by in house developed software. The peptide mass was compared with theoretic peptide masses of all available proteins from all species. The monoisotopic mass was used and a mass tolerence of 0.002596 was allowed. 4 matching peptides were the minimal requirement for an identity assignment. Mismatch or miscleavage sites were not considered.

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Table 1: Clinical and histopathological characteristics of samples

No. of Samples Samples Samples Samples Samples Samples Samples PC-01 Male G8 Head of Poorly differentiate pancreas adenocarcinoma Ad						
Male 68 Head of pancreas Male 68 Head of pancreas Male 44 Head of pancreas Pemale 65 Head of pancreas Pemale 65 Head of pancreas Remale 65 Head of pancreas Pemale 59 Head of pancreas Pemale 54 Head of pancreas Pemale 54 Head of pancreas Pemale 54 Head of pancreas Pemale 65 Head of pancreas Pemale 65 Head of pancreas Pemale 64 Head of pancreas Pemale 65 Head of pancreas Pemale 66 Head of pancreas	No. of Samples	Sex	Age	Tumor location	Histology	Metastasis in lymph nodes
Male 68 Head of Pancreas Male 44 Head of Pancreas Male 66 Head of Pemale 65 Head of Pancreas Remale 65 Head of Pancreas Male 59 Head of Pemale 62 Body of Pemale 54 Head of Pemale 54 Head of Pemale 55 Head of Pemale 65 Head of Pemale 65 Head of Pemale 65 Head of Pemale 66 Head of Pemale 67 Head of Pemale 68 Head of Pemale 69 Head of Pemale 69 Head of	PC-01	Male	48	Head of pancreas	Middle differentiated ductal adenocarcinoma	Yes
Male 44 Head of pancreas Male 66 Head of pancreas Female 45, Head of pancreas Male 59 Head of pancreas Male 54 Head of pancreas Female 55 Head of pancreas	PC-02	Male	89	Head of pancreas	Poorly differentiated adenocarcinoma	Yes
Male 66 Head of pancreas Female 45, Head of pancreas Pemale 65 Head of pancreas Male 59 Head of pancreas Male 54 Head of pancreas Female 53 Head of pancreas Female 54 Head of pancreas Female 54 Head of pancreas Female 69 Head of pancreas	PC-03	Male	44	Head of pancreas	Poorly differentiated ductal adenocarinoma, clear cell type	Yes
Female45.Head of pancreasPemale65.Head of pancreasMale59.Head of pancreasFemale62.Body of pancreasPemale54.Head of pancreasFemale53.Head of pancreasFemale54.Head of pancreasFemale69.Head of pancreasFemale69.Head of pancreas	PC-04	Male	.99	Head of pancreas	Well differentiated ductal adenocarcinoma	Yes
Pemale 65 Head of pancreas Male 59 Head of pancreas Female 62 Body of pancreas Male 54 Head of pancreas Female 53 Head of pancreas Female 69 Head of pancreas	C-05	Female	45,	Head of pancreas	Well differentiated ductal adenocarcinoma	No O
Male 59 Head of Pancreas Remale 62 Body of Pancreas Male 54 Head of Pancreas Female 53 Head of Pancreas Female 69 Head of Pancreas	SC-06	Female	92	Head of pancreas	Well differentiated ductal adenocarcinoma	Yes
Female62Body ofMale54Head ofPemale53Head ofPemale54Head ofPemale54Head ofPemale69Head ofPemale69Head of	C-07	Male	59	Head of pancreas	Middle differentiated ductal adenocarcinoma	Yes
Male 54 Head of Pancreas Remale 53 Head of pancreas Female 54 Head of pancreas Female 69 Head of pancreas	2C-08	Female	62	Body of pancreas	Well differentiated ductal adenocarcinoma	Yes
Pemale 53 Head of pancreas Female 54 Head of pancreas Female 69 Head of pancreas	60-0	Male	. 55	Head of pancreas	Middle differentiated ductal adenocarcinoma	No
Female 54 Head of pancreas Female 69 Head of	C-10	Pemale	53	Head of pancreas	Well differentiated ductal adenocarcinoma	No O
Female 69 Head of pancreas	·C-11	Female	24	Head of pancreas	Middle differentiated ductal adenocarcinoma	Yes
	C-12	Female	69	Head of pancreas	Middle differentiated ductal adenocarcinoma	Yes

- 23 -Table 2: Proteins up-regulated in pancreatic cancer I

sw.CATD_HUMAN P07339 Cathepain D precursor (ce 3.4.23.5). 1 <2	Protein	Acc No	Description	Seq ID No.	Pold Change
P06396 Gelsolin precursor, plasma 3	sw:CATD_HUMAN	P07339	Cathepsin D precursor (ec 3.4.23.5).	-	å
P06396 Geleolin precursor, plasma 3 P00751 Complement factor B precursor (ec 3.4.21.47) 4 O43707 Alpha-actinin 4 (non-muscle alpha-actinin 4) 5 P12814 Alpha-actinin 1 (alpha-actinin cytoskeletal isoform) 7 P05215 Tubulin alpha-4 chain. 8 P07216 Tubulin alpha-4 chain. 8 P07226 Transgelin 2 (smooth muscle protein 22-alpha) 10 P07226 Transgelin 2 (smooth muscle protein 22-alpha) 10 P07226 Transforming growth factor-beta induced of protein 1G-H3 precursor 6 Q05524 Alpha enolase 12 Q05524 Alpha enolase 13 Q05154 Aminoacylase-1 14 P47756 P-actin capping protein beta subunit (capz beta) 15 Q15181 Inorganic pyrophosphatase 16 P17931 Galectin-3 (galactose-specific lectin 3). 17	sw:IDHC_HUMAN	075874	Isocitrate dehydrogenase [NADP] cytoplasmic (ec 1.1.1.1.2)	2	. 2
P00751 Complement factor B precursor (ec 3.4.21.47) 4 O43707 Alpha-actinin 4 (non-muscle alpha-actinin 4) 5 P12814 Alpha-actinin 1 (alpha-actinin cytoskeletal isoform) 7 P05215 Tubulin alpha-4 chain. 8 P1333 Filamin A (Endothelial actin-binding protein) 9 P07226 Transgelin 2 (smooth muscle protein 22-alpha) 10 P07226 Tropomyosin alpha 4 chain 111 Q05524 Transforming growth factor-beta induced 6 Q05524 Alpha enolase 13 Q05524 Alpha enolase 13 Q05554 Aminoacylase-1 14 P47756 P-actin capping protein beta subunit (capz beta) 15 Q15181 Inorganic pyrophosphatase 16 P17931 Galectin-3 (galactose-specific lectin 3). 17	sw:GELS_HUMAN	P06396	Gelsolin precursor, plasma	6	Э.
043707 Alpha-actinin 4 (non-muscle alpha-actinin 4) 5 P12814 Alpha-actinin 1 (alpha-actinin cytoskeletal isoform) 7 P05215 Tubulin alpha-4 chain. 8 P21333 Filamin A (Endothelial actin-binding protein) 9 P07226 Transgelin 2 (smooth muscle protein 22-alpha) 10 P07226 Tropomyosin alpha 4 chain 11 Q05582 Transforming growth factor-beta induced 6 protein IG-H3 precursor 6 Q05582 Alpha enolase 13 Q05584 Aminoacylase-1 14 P47756 P-actin capping protein beta subunit (capz beta) 15 Q15181 Inorganic pyrophosphatase 16 P17931 Galectin-3 (galactose-specific lectin 3). 17	8w:CFAB_HUMAN	P00751	Complement factor B precursor (ec 3.4.21.47)	4	3
P12814 Alpha-actinin 1 (alpha-actinin cytoakeletal 7	SW:AAC4_HUMAN	043707	Apha-actinin 4 (non-muscle alpha-actinin 4)	2	7
P05215 Tubulin alpha-4 chain. 8 P21333 Filamin A (Endothelial actin-binding protein) 9 P37802 Transgelin 2 (smooth muscle protein 22-alpha) 10 P07226 Tropomyosin alpha 4 chain 11 Q15582 Transforming growth factor-beta induced 6 P17554 Armaforming growth factor-beta induced 6 Q05582 Caldesmon (cdm) 12 Q05584 Alpha enolase 13 Q05584 Aminoacylase-1 14 P47756 P-actin capping protein beta aubunit (capz beta) 15 Q15181 Inorganic pyrophosphatase 16 P17931 Galectin-3 (galactose-specific lectin 3). 17	sw:AAC1_HUMAN	P12814	Apha-actinin 1 (alpha-actinin cytoskeletal isoform)	7	2
P21333 Filamin A (Endothelial actin-binding protein) 9 P37802 Transgelin 2 (smooth muscle protein 22-alpha) 10 P07226 Tropomyosin alpha 4 chain 11 Q15582 Transforming growth factor-beta induced 6 Protein IG-H3 precursor 6 Q05582 Caldesmon (cdm) 12 Q05524 Alpha enolase 13 Q05524 Aminoacylase-1 14 P47756 P-actin capping protein beta subunit (capz beta) 15 Q15181 Inorganic pyrophosphasase 16 P17931 Galectin-3 (galactose-specific lectin 3). 17	sw:TBA4_HUMAN	P05215	Tubulin alpha-4 chain.	. 80	2
P37802 Transgelin 2 (amooth muscle protein 22-alpha) 10 P07226 Tropomyosin alpha 4 chain 11 Q15582 Transforming growth factor-beta induced 6 Q05682 Caldesmon (cdm) 12 Q05524 Alpha enolase 13 Q05154 Aminoacylase-1 14 P47756 P-actin capping protein beta subunit (capz beta) 15 Q15181 Inorganic pyrophosphatase 16 P17931 Galectin-3 (galactose-specific lectin 3). 17	6W:ABP2_HUMAN	P21333	Filamin A (Endothelial actin-binding protein)	6	4
P07226 Tropomyosin alpha 4 chain 11 11 11 11 12 12 12 1	sw:TAGL_HUMAN	P37802	Transgelin 2 (smooth muscle protein 22-alpha)	10	7
Q15582 Transforming growth factor-beta induced protein IG-H3 precursor 6 Q05682 Caldesmon (cdm) 12 Q05524 Alpha enolase 13 Q05154 Aminoacylase-1 14 P47756 P-actin capping protein beta subunit (capz beta) 15 Q15181 Inorganic pyrophosphatase 16 P17931 Galectin-3 (galactose-specific lectin 3). 17	sw:TPM4_HUMAN	P07226	Tropomyosin alpha 4 chain	11	Ø
Q05682 Caldesmon (cdm) 12 Q05524 Alpha enolese 13 Q05154 Aminoacylase-1 14 P47756 P-actin capping protein beta subunit (capz beta) 15 Q15181 Inorganic pyrophosphatase 16 P17931 Galectin-3 (galactose-specific lectin 3). 17	8w:BGH3_HUMAN	Q15582	Transforming growth factor-beta induced protein IG-H3 precursor	9	'n
Q05524 Alpha enolase 13 Q03154 Aminoacylase-1 14 P47756 F-actin capping protein beta subunit (capz beta) 15 Q15181 Inorganic pyrophosphatase 16 P17931 Galectin-3 (galactose-specific lectin 3). 17	8w:CALD_HUMAN	Q05682	Caldesmon (cdm)	12	2
Q03154 Aminoacylase-1 14 P47756 P-actin capping protein beta subunit (capz beta) 15 Q15181 Inorganic pyrophosphatase 16 P17931 Galectin-3 (galactose-specific lectin 3) 17	sw:ENOL_HUMAN	Q05524	Alpha enolase	13	7
P47756 F-actin capping protein beta subunit (capz beta) 15 Q15181 Inorganic pyrophosphatase 16 P17931 Galectin-3 (galactose-specific lectin 3). 17	8W:ACY1_HUMAN	Q03154		41	c,
Q15181 Inorganic pyrophosphatase 16 P17931 Galectin-3 (galactose-specific lectin 3). 17	sw:CAPB_HUMAN	P47756	P-actin capping protein beta subunit (capz beta)	51	. 5
P17931 Galectin-3 (galactose-specific lectin 3). 17	swiPYR_HUMAN	Q15181	Inorganic pyrophosphatase	91	۵
	sw.LEG3_HUMAN	P17931	Galectin-3 (galactose-specific lectin 3).	17.	2

Q

Voltage-dependent anion-selective channel

protein 2

P45880

8w:POR2_HUMAN

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19 20

P50454 | Collagen-binding protein 2 precursor

P07355 Annexin II

SW:ANX2_HUMAN sw:CBP2_HUMAN sw:COF1_HUMAN

P23528 Cofilin, non-muscle isoform

Q Q

77 22 23 24

7

Delta3,5-Delta2,4-dienoyl-coa isomerase,

mitochondrial precursor

8W.ECH1_HUMAN Q13011

Q13409 Dynein intermediate chain 2, cytosolic

sw:DY12_HUMAN

sw.CYPH_HUMAN | P05092 | Peptidyl-prolyl cis-trans isomerase A

7

56 27

48

sw:MLRN_HUMAN | P24844 | Myosin regulatory light chain 2

P13796 | L-Plastin

sw.PLSL_HUMAN

Ç 7

28 53

Q07244 | Heterogeneous nuclear ribonucleoprotein k

sw:ROK_HUMAN

P13693 Translationally controlled tumor

sw:TCTP_HUMAN

sw:RAN_HUMAN | P17080 | GTP-binding nuclear protein ran

30

33 33 33 * 35 38

sw:TYPH_HUMAN | P19971 | Thymidine phosphorylase precursor

P28838 Cytosol aminopeptidase

sw:AMPL_HUMAN

sw:TPM1_HUMAN | P09493 | Tropomyosin I alpha chain

P08727 Keratin, type i cytoskeletal 19 (cytokeratin 19)

8w:K1CS_HUMAN

sw:ALDX_HUMAN | P14550 | Alcohol dehydrogenase (NADP+)

P09093 Blastase IIIa precursor

sw:EL3A_HUMAN

37 38

P30084 | Enoyi-CoA hydratase, mitochondrial precursor

sw.ECHM_HUMAN

Dihydrolipoamide dehydrogenase,

mitochondrial precursor

P09622

sw:DLDH_HUMAN

sw.HSBX_HUMAN | 014558 | Heat-shock 20 kDa like-protein p20.

MANUAL MODERN
F104/5
P27824
Q07021
P28331
P43490
P09455
P49368
P13489
P25388
P06702

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SW:MLEN_HUMAN	P16475	Myosin light chain alkali, non-muscle isoform	39	9
sw:CALX_HUMAN	P27824	Calnexin precursor	40	
sw:MA32_HUMAN	Q07021	Complement component 1	14	Q
SW:NUAM_HUMAN	P28331	NADH-ubiquinone oxidoreductase 75 kda subunit, mitochondrial precursor	42	7.
EW:PBEP_HUMAN	P43490	Pre-B cell enhancing factor precursor.	43	2
sw:RET1_HUMAN	P09455	Retinol-binding protein I, cellular	44	2
sw.TCPG_HUMAN	P49368	T-complex protein 1, gamma subunit	45	2
sw.RINI_HUMAN	P13489	Placental ribonuclease inhibitor	46	4
sw:GBLP_HUMAN	P25388	Guanine nucleotide-binding protein beta subunit-iike protein 12,3	47	2
FW:S109_HUMAN	P06702	Calgranulin B	49	å

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Table 4. Proteins roughly classified by their involved biological processing or basic function

Table 3: Proteins up-regulated in pancreatic cancer II

Protein	Acc No	Description	Seq ID	Fold .
			2	Similar
sw:CAPG_HUMAN	P40121	Macrophage capping protein	S.	eż.
sw.ANX1_HUMAN	P04083	Annertn I (lipocortin I) (calpactin II)	51	4
8W:K2C7_HUMAN	P08729	Keratin, type II cytoskeletal 7	52	s,
humangp:CHR13- Q15063	Q15063	Osteoblast specific factor 2 precursor	53	2
sw.TGLC_HUMAN	P21980	Protein-glutamine gamma-glutamyltransferase	54	7
8w:GDIR_HUMAN	P52565	Rho GDP-dissociation inhibitor 1	55	4
swIQG1_HUMAN	P46940	Ras GTPase-activating-like protein	25	7

otein function"	Number ^b	Percentage (%) ^C
tructural constitural and regulation of cytoskeleton	19	20.8
Cell cycle and metabolism	74	25.3
Response to external stimulus or stress	19	20.8
Signal transduction	13	7,7
Nuclear function	18	6.1
Transport processing	19	6.5
Hemostatis	12	1.4
Cell adhension	7	2.4
Chaperon	7	2.4
Apoptosis	9	-
Unknown function	111	3.7
Others		2.4
Total	293	100

Table 5. Proteins with higher levels in normal pancreatic compared to cancer tissue

HUMAN P17661 P17661 P17661 P17661 P15086 P15086 P15086 P15086 P17538 P07477 P07477 P07477 P07477 P10MAN P10809 P10MAN P10809 P10MAN P100809	desmin. d peptidolysis carboxypeptidase b precursor carboxypeptidase al precursor carboxypeptidase a2 precursor carboxypeptidase a2 precursor carboxypeptidase a2	3 2 2 Uncalc	72 72 73 73 74 74 74
10MAN	desmin. peptidolysis roxypeptidase b precursor carboxypeptidase al precursor carboxypeptidase a2 precursor choxypeptidase a2 choxypeptidase a2 choxypeptidase a2 precursor chymotrypainogen b	2 2 Uncalc ulated Uncalc Uncalc Uncalc ulated Uncalc ulated	72 73 73 73 75 75 75 75 75 75 75 75 75 75 75 75 75
Proteolysis and Proteolysi	rboxypepidase b precursor carboxypepidase al precursor carboxypepidase a2 precursor carboxypepidase a2 precursor chymotrypainogen b	2 Uncalc ulated ulated ulated Uncalc ulated ulated ulated ulated	71 72 72 73 74 74 75
HUMAN P15086 HUMAN P50454 HUMAN P07477 HUMAN P10809 HUMAN P10809 HUMAN P30040 HUMAN P30040 HUMAN P30101 HUMAN P30101	carboxypeptidase b precursor carboxypeptidase a1 precursor carboxypeptidase a2 precursor chymotrypatinogen b precursor	2 Uncalc ulated ulated Uncalc ulated ulated ulated	73 73 74 74 75
TUMAN P15085 HUMAN P17538 HUMAN P07477 HUMAN P18089 HUMAN P14625 HUMAN P14625 HUMAN P30040 HUMAN P30101 HUMAN P30101	carboxypepildase al pretursor carboxypepildase a2 pretursor chymotrypainogen b	Uncalc ulated Uncalc ulated ulated ulated	73 74 75
HUMAN P50454 HUMAN P07477 HUMAN P07478 HUMAN P10809 HUMAN P14625 HUMAN P30040 HUMAN P30101 HUMAN P30101 HUMAN P30101	carboxypeptidase a2 precursor chymotrypsinogen b precursor	Uncalc ulated Uncalc ulated Uncalc ulated	73 74 75
HUMAN P07478 HUMAN P07478 HUMAN P10809 HUMAN P30040 HUMAN P30040 HUMAN P30040 HUMAN P30055 HUMAN P30101 HUMAN P30101	chymotrypsinogen b precursor	Uncalc ulated Uncalc ulated	74
HUMAN P07477 HUMAN P10809 HUMAN P10825 HUMAN P30040 HUMAN P30101 HUMAN P30101 HUMAN P30101		Uncalc ulated	75
HUMAN P30740 HUMAN P10809 HUMAN P30040 HUMAN P30040 HUMAN P30101 HUMAN P30101	trypsin i precursor (ec 3.4.21.4) (cationic trypsinogen).		
HUMAN P30740 HUMAN P14625 HUMAN P30040 HUMAN Q13087 HUMAN P30101 HUMAN P90325	trypsin ii precursor (anionic trypsinogen).	m .	76
HUMAN P10809 P14625 HUMAN P30040 HUMAN Q13087 P30101 P3010	leukocyte elastase inhibitor	4	77
HUMAN P14625 HUMAN P30040 HUMAN Q13087 I HUMAN P30101 I			
	human, mitochondrial matrix protein p1 precursor	7	78
HUMAN P30040 HUMAN P30101 1 HUMAN P30101 1	94 kda glucose-regulated protein	6	79
HUMAN P30101 1	endoplasmic reticulum protein erp29 precursor	7	80
HUMAN P30101 1	protein disulfide isomerase a2 precursor	2	81
HUMAN P00325	protein disulfide isomerase a3 precursor	2	82
P00325			
	alcohol dehydrogenase beta chain	4	83
sw.GTO1_HUMAN P78417 glu	glutathione transferase omega l	Uncalc ulated	84
sw:OXRP_HUMAN Q9Y4L1	150 kda oxygen-regulated protein precursor	Uncalc	85

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8w:PDX4_HUMAN	Q13162	peroxiredoxin 4	4	98
sw:ULA4_HUMAN	P30039	mawd binding protein	ø	87
metabolism of biological process	2			
sw:AMYC_HUMAN	P19961	alpha-amylase 2b precursor	"	88
sw:AMYP_HUMAN	P04746	alpha-amylase, pancreatic precursor	Uncalc ulated	68
sw:ATPA_HUMAN	P25705	atp synthase alpha chain, mitochondrial precursor	۵.	8
sw:BAL_HUMAN	P19835	bile-salt-activated lipase precursor	6	16
sw:LIP1_HUMAN	P54315	pancreatic lipase related protein 1 precursor.	Q	82
8w:LIP2_HUMAN	P54317	pancreatic lipase related protein 2 precursor	Uncalc ulated	g
sw:LIPP_HUMAN	P16233	triacylglycerol lipase, pancreatic precursor	Uncalc ulated	96
8w:DPYZ_HUMAN	Q16555	dihydropyrimidinase related protein-2		. 28
sw:GABT_HUMAN	P80404	4-aminobutyrate aminotransferase	2	96
sw:GATM_HUMAN	P50440	glycine amidinotransferase, mitochondrial precursor	Uncalç ulated	76
sw:GR78_HUMAN	P11021	78 kda glucose-regulated protein precursor (grp 78)	e .	8
sw:IF32_HUMAN	Q13347	eukaryotic translation initiation factor 3 subunit 2	4	8
sw:DPY2_HUMAN	Q16555	dihydropyrimidinase related protein-2		100
8W:PGMU_HUMAN	P36871	phosphoglucomutase	2	101
8w:PSA1_HUMAN	P25786	proteasome subunit alpha type 1	7	102
heat shock protein				
fw:HS27_HUMAN	P04792	heat shock 27 kda protein	Uncalc	103
signaling				
SW:PD61	Q8WUM4	programmed cell death 6 interacting protein	ī,	104
muscle development].

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91 8 <u>8</u> 101 Uncalç ulated 5 a Skeletal muscle LIM-protein 2 (SLIM 2)(Four and a half LIM domains protein 3)(FHL.3), four and a half lim domains 3 collagen alpha 1(vi) chain precursor. pancreatitis-associated protein 1 precursor. lumican precursor cytochrome b5. Q06141 Q13643 P00167 P12109 P51884 transport of biological process SW:CA16_HUMAN sw.CYB5_HUMAN SW:LUM_HUMAN hsugp:057687-10-0 sw:PAP1_HUMAN SW:sli2 cell adhesion

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Table 6 Proteins with higher levels in pancreatic cancer compared to in normal tissue

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Protein *	AccNob	Description	Fold	Seq ID No.
cytoskeletal regulation				
sw:PSC2_HUMAN	014926	fascin 2 (retinal fascin).	2	35
sw.AAC!_HUMAN	P12814	alpha-actinin i	2	7
sw.AAC4_HUMAN	043707	alpha-actinin 4	7	5
sw.ABP2_HUMAN	P21333	endothelial actin-binding protein (alpha-filamin).	4	ō
sw.ANX2_HUMAN	P07355	human annexin ii (lipocortin ii)	2	61
sw:CALD_HUMAN	Q05682	caldesmon (cdm).	7	12
sw:CAPB_HUMAN	P47756	f-actin capping protein beta subunit	r.	15
sw:CAPG_HUMAN	P40121	macrophage capping protein	6	8
sw:COFI_HUMAN	P23528	cofilin, non-muscle isoform (p18).	Ø	21
sw.DBST_HUMAN	P18282	destrin (actin-depolymerizing factor) (adf).	7	57
sw.DY12_HUMAN	Q13409	dynein intermediate chain 2(fragment).	2	23
sw:GELS_HUMAN	P06396	gelsolin precursor	9	3
swKiCS_HUMAN	P08727	keratin, type i cytoskeletal 19	4	33
sw:K2C7_HUMAN	P08729	keratin, type ii cytoskeletal 7	5	52
sw:MLEN_HUMAN	P16475	myosin light chain alkali	9	39
sw:PLSL_HUMAN	P13796	l-plastin (lymphocyte cytosolic protein 1)	4	26 .
sw:TAGL_HUMAN	P37802	transgelin (22 kda actin-binding protein).	7	01
sw:TBA4_HUMAN	P05215	tubulin alpha-4 chain.	7	∞ .
proteolysis and peptidolysis			-	
sw.ACY1_HUMAN	Q03154	aminoacylase-1	\$.	14
sw.AMPL_HUMAN	P28838	cytosol aminopeptidase	6	32
sw:CATD_HUMAN	P07339	cathepsin d precursor.	7	-
				1

w:CPAB_HUMAN	P00751	complement factor b precursor	2	4	
w:BL3A_HUMAN	P09093	elastase ilia precursor	4	35	
haperon					
w:APE_HUMAN	P02649	apolipoprotein e precursor (apo-e).	2	59	
w:CALX_HUMAN	P27824	calnexin precursor(p90)	6	6	
m:CYPH_HUMAN	P05092	peptidyi-prolyi cis-trans isomerase a	a	22	
w:TCPG_HUMAN	P49368	t-complex protein 1, gamma subunit	7	45	
w:CBP2_HUMAN	P50454	human. collagen-binding protein 2 precurso	2	20	
_hum:Q96C61	1996061	hypothetical 88.6 kda protein	2	99	
xidoreductase					
w:DLDH_HUMAN	P09622	dihydrolipoamide dehydrogenase	2	36	
widhc_human*	075874	isocitrate dehydrogenase [nadp] cytoplasmic	7	2	
w:NUAM_HUMAN	P28331	nadh-ubiquinone oxidoreductase 75 kda subunit	2	42	
netabolism of biological process] 88		1		
W.ALDX_HUMAN	P14550	alcohol dehydrogenase [nadp+]	4	34	
#BCH1_HUMAN	Q13011	delta3,5-delta2,4-dienoyl-coa isomerase	7	24	
w.ECHM_HUMAN	P30084	enoyl-coa hydratase, mitochondrial precursor	6	37	
MIPYR_HUMAN	Q15181	inorganic pyrophosphatase	2	91	
M:TYPH_HUMAN	P19971	thymidine phosphorylase precursor	z.	31	
W:ENOA_HUMAN	P06733	human alpha enolase	2	19	
wENOL_HUMAN	Q05524	alpha enolase, lung specific	7	13	
w:SYW_HUMAN	P23381	tryptophanyl-tma synthetase	7	62	
eat shock protein					÷
w:HSBX_HUMAN	014558	heat-shock 20 kda like-protein p20.	7	38	
ignaling					
#:GBLP_HUMAN	P25388	guanine nucleotide-binding protein beta subunit-like protein 12.3	7	47	
			1		

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sw:GDIR_HUMAN	P52565	rho gdp-dissociation inhibitor i	4	55
sw:IQG1_HUMAN	P46940	ras grpase-activating-like protein iqgap i	7	25
8w.PBEP_HUMAN	P43490	pre-b cell enhancing factor precursor.	7	43
sw:RAN_HUMAN	P17080	gtp-binding nuclear protein ran	E .	7.7
immune response				
sw:KAC_HUMAN	P01834	ig kappa chain c region.	2	63
8w:MA32_HUMAN	Q07021	pre-mma splicing factor sf2, p32 subunit.	Q	41
inflammatory reponse				
sw:ANX1_HUMAN	P04083	annexin i (lipocortin i)	*	51
ew.LBG3_HUMAN	P17931	galectin-3	7	17
sw:S109_HUMAN	P06702	calgranulin b (mrp-14)	7	49
muscle development				
sw:TPM1_HUMAN	P09493	tropomyosin i alpha chain	2	23
sw.TPM4_HUMAN	P07226	tropomyosin alpha 4 chain	4	=
sw:MLRN_HUMAN	P24844	myosin regulatory light chain 2	7	84
transport of biological process				
humangp:CHR2-Q15092	Q15092	transmembrane protein.	7	64
sw:POR2_HUMAN	P45880	voltage-dependent anion-selective channel protein 2	۵.	18
sw:RET1_HUMAN	P09455	retinol-binding protein I	2	2
RNA processing				
humangp:CHR20-Q9P2E9	075300	ribosome binding protein 1 (kiaa 1398 protein).	4	59
sw:RINI_HUMAN	P13489	placental ribonuclease inhibitor	9	46
sw:ROK_HUMAN	Q07244	heterogeneous nuclear ribonucleoprotein k	7	78
blood coagulation				
*w.PIBG_HUMAN	P02679	fibrinogen gamma chain precursor	6	8
sw.THRB_HUMAN	P00734	prothrombin precursor	۵.	29
Anti-apoptosis				

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	D13603	translationally controlled tumor	7	59
sw:TCTP_HUMAN	110011	protein (p23)	7	
cell adhesion				
humangp:CHR13-Q15063	Q15063	osteoblast specific factor 2 precursor	7	53
sw:BGH3_HUMAN	Q15582	transforming growth factor-beta induced protein	s	9
other				
sw:TGLC_HUMAN	P21980	P21980 tissue transglutaminase	7	54
8w:KPY1_HUMAN	P14618	Human pyruvate kinase, cytosolic thyroid hormone-binding protein	E.	89
humangp:CHR19-Q96D15	510960	Q96D15 Reticulocalbin 3 precursor.	2	69

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Claims

- A marker for diagnosis of pancreatic cancer comprising at least one polypeptide selected from the group consisting of the polypeptides listed in tables 2 and 3.
- 5 2. The marker of claim I wherein the group from which at least one polypeptide is selected consists of the polypeptides listed in table 2.
- 3. A polypeptide selected from the group consisting of the polypeptides listed in tables 2 and 3, for use as a marker or as a component of a marker for diagnosis of pancreatic
 - 10 cancer and/or the susceptibility to pancreatic cancer.
- An in vitro method for the diagnosis of pancreatic cancer and/or the susceptibility to pancreatic cancer comprising the steps of
- a) obtaining a biological sample; and
- b) detecting and/or measuring the increase of a marker of claims 1 or 2.

- The in vitro method of claim 4, wherein the marker comprises at least two polypeptides.
- 20 6. The in vitro method of claims 4 or 5 wherein said biological sample is derived from the group consisting of serum, plasma, pancreatic juice and cells of pancreatic tissue.
- An in vitro method for the diagnosis of pancreatic cancer and/or the susceptibility to pancreatic cancer comprising the steps of
- 25 a) obtaining a biological sample; and
- b) detecting and/or measuring the increase of at least one nucleic acid coding for the marker of claims 1 or 2.

PCT/EP2003/014057 38 The in vitro method of claim 7, wherein said nucleic acid molecule is RNA or DNA. œ.

The in vitro method of claim 8, wherein said DNA is a cDNA. ٥.

The in vitro method of any one of claims 7 to 9, wherein the expression levels of at least one of said nucleic acids in an individual suspected to suffer from pancreatic cancer and/or to be susceptible to pancreatic cancer is compared to the expression levels of the same nucleic acids in a healthy individual. 9

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The in vitro method of any one of claims 4 to 6, wherein the expression level of said susceptible to pancreatic cancer is compared to the expression levels of the same marker marker in an individual suspected to suffer from pancreatic cancer and/or to be in a healthy individual. ::

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- The in vitro method of claim 11, wherein an increase of the expression levels of said marker is indicative of pancreatic cancer or the susceptibility to pancreatic cancer. 12.
- A screening method for identifying and/or obtaining a compound which interacts with a polypeptide listed in tables 2 and/or 3 whose expression is upregulated in pancreatic cancer, comprising the steps of 13. 20
- under conditions which allow interaction of said compound with said polypeptide; a) contacting said polypeptide with a compound or a plurality of compounds
- b) detecting the interaction between said compound or plurality of compounds with said polypeptide. 25

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inhibitor or an antagonist of a polypeptide listed in tables 2 and/or 3 whose expression is 14. A screening method for identifying and/or obtaining a compound which is an upregulated in pancreatic cancer, comprising the steps of

- the screening method of claim 13 under conditions which allow interaction of said a) contacting a said polypeptide with a compound identified and/or obtained by compound with said polypeptide;
- b) determining the activity of said polypeptide;
- c) determining the activity of said polypeptide expressed in the host as defined in (a), which has not been contacted with said compound; and
- decreased activity determined in (b) in comparison to (c) is indicative for an d) quantitatively relating the activity as determined in (b) and (c), wherein a inhibitor or antagonist.
- inhibitor of the expression of a polypeptide listed in tables 2 and/or 3 whose expression is 15. A screening method for identifying and/or obtaining a compound which is an upregulated in pancreatic cancer, comprising the steps of 2
- a) contacting a host which expresses said polypeptide with a compound,
- b) determining the expression level and/or activity of said polypeptide;
- c) determining the expression level and/or activity of said polypeptide in the host as defined in (a), which has not been contacted with said compound; and

- d) quantitatively relating the expression level of said polypeptide as determined in
- (b) and (c), wherein a decreased expression level determined in (b) in comparison
 - to (c) is indicative for an inhibitor of the expression of said polypeptide.
- 25 16. A compound identified and/or obtained by the screening methods of any one of claims 13 to 15.
- 17. A pharmaceutical composition comprising the compound of claim 16.

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comprising formulating the compound of claim 16 in a pharmaceutically acceptable 18. A method for the preparation of the pharmaceutical composition of claim 17 carrier or diluent.

- 19. Use of a compound of claim 16 for the preparation of a medicament for the treatment or prevention of pancreatic cancer.
- Use of a compound of claim 16 for the preparation of a diagnostic composition for diagnosing pancreatic cancer or a predisposition for pancreatic cancer. 20.

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- The use of claim 19 or 20 wherein said compound comprises an antibody, an antibody-derivative, an antibody fragment, a peptide or an antisense construct. 21.
- 22. Antibodies against the proteins listed in tables 2 and/or 3, or antigen-binding fragments thereof, for the use in an in vitro method for the diagnosis of pancreatic cancer, 12
- 23. A kit for the diagnosis of pancreatic cancer comprising one or more of the antibodies, or antigen-binding fragments thereof, of claim 22.

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- 24. A kit for the diagnosis of pancreatic cancer comprising one or more of the nucleic acids coding for the marker of claims 1 or 2.
- 25. A kit for screening of compounds that activate or inhibit any of the polypeptides listed in tables 2 and/or 3, or stimulate or inhibit the expression of any of said polypeptides. 52

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26. A marker for diagnosis of pancreatic cancer comprising at least one polypeptide selected from the group consisting of the polypeptides listed in table 6.

- The marker of daim 26, wherein said at least one polypeptide does not include Seq.
 ID No.s 25 and 50 to 55.
- 28. The marker according to any one of claims 26 to 27, additionally comprising at least one of the polypeptides listed in table 5.
- 29. An in vitro method for the diagnosis of pancreatic cancer and/or the susceptibility to pancreatic cancer comprising the steps of 2
- a) obtaining a biological sample; and
- b) detecting and/or measuring the increase of at least one of the polypeptides listed in table 6.

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- The in vitro method of claim 29, additionally comprising the step of detecting and/or measuring the decrease of at least one of the polypeptides listed in table 5. . 9
- The in vitro method of claims 29 or 30, wherein said at least one polypeptide does not include Seq ID No.s 25 and 50 to 55. 31. 2
- The in vitro method of any one of claims 29 to 31, wherein said biological sample is derived from the group consisting of serum, plasma, pancreatic juice and cells of pancreatic tissue. 32.

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33. An in vitro method for the diagnosis of pancreatic cancer and/or the susceptibility to pancreatic cancer comprising the steps of

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- a) obtaining a biological sample; and
- b) detecting and/or measuring the increase of at least one nucleic acid coding for the marker of any one of claims 26 to 28.
- 5 34. The in vitro method of claim 33, wherein said nucleic acid molecule is RNA or DNA.
- 35. The in vitro method of claim 34, wherein said DNA is a cDNA.
- 10 36. The in vitro method of any one of claims 33 to 35, wherein the expression levels of at least one of said nucleic acids in an individual suspected to suffer from pancreatic cancer and/or to be susceptible to pancreatic cancer is compared to the expression levels of the same nucleic acids in a healthy individual.
- 15 37. The in vitro method of any one of claims 33 to 36, wherein the expression level of said marker in an individual suspected to suffer from pancreatic cancer and/or to be susceptible to pancreatic cancer is compared to the expression levels of the same marker in a healthy individual.
- 20 38. The in vitro method of claim 37, wherein an increase of the expression levels of said marker is indicative of pancreatic cancer or the susceptibility to pancreatic cancer.
- 39. A screening method for identifying and/or obtaining a compound which interacts with a polypeptide selected from the group consisting of the polypeptides listed in table 6
 25 whose expression is upregulated in pancreatic cancer, comprising the steps of
- a) contacting said polypeptide with a compound or a plurality of compounds under conditions which allow interaction of said compound with said polypeptide;
 and

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 b) detecting the interaction between said compound or plurality of compounds with said polypeptide.

- 40. A screening method for identifying and/or obtaining a compound which is an
 - inhibitor or an antagonist of a polypeptide listed in table 6 whose expression is upregulated in pancreatic cancer, comprising the steps of
- a) contacting said polypeptide with a compound identified and/or obtained by the screening method of claim 39 under conditions which allow interaction of said compound with said polypeptide;
- b) determining the activity of said polypeptide;
- c) determining the activity of said polypeptide expressed in the host as defined in (a), which has not been contacted with said compound; and
- d) quantitatively relating the activity as determined in (b) and (c), wherein a decreased activity determined in (b) in comparison to (c) is indicative for an
 - 15 inhibitor or antagonist.
- 41. A screening method for identifying and/or obtaining a compound which is an inhibitor of the expression of a polypeptide selected from the group consisting of the polypeptides listed in table 6 whose expression is upregulated in pancreatic cancer,
 - 20 comprising the steps of
- a) contacting a host which expresses said polypeptide with a compound,
- b) determining the expression level and/or activity of said polypeptide;
- c) determining the expression level and/or activity of said polypeptide in the host as defined in (a), which has not been contacted with said compound; and
- d) quantitatively relating the expression level of said polypeptide as determined in (b) and (c), wherein a decreased expression level determined in (b) in comparison to (c) is indicative for an inhibitor of the expression of said polypeptide.

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42. A compound identified and/or obtained by the screening methods of any one of claims 39 to 41.

43. A pharmaceutical composition comprising the compound of claim 42.

comprising formulating the compound of claim 42 in a pharmaceutically acceptable 44. A method for the preparation of the pharmaceutical composition of claim 43 carrier or diluent.

10 45. Use of a compound of claim 42 for the preparation of a medicament for the treatment or prevention of pancreatic cancer. 46. Use of a compound of claim 42 for the preparation of a diagnostic composition for diagnosing pancreatic cancer or a predisposition for pancreatic cancer.

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The use of claim 45 or 46 wherein said compound comprises an antibody, an antibody-derivative, an antibody fragment, a peptide or an antisense construct. 47.

48. Antibodies against the proteins listed in tables 5 and/or 6, or antigen-binding fragments thereof, for the use in an in vitro method for the diagnosis of pancreatic 20

49. A kit for the diagnosis of pancreatic cancer comprising one or more of the antibodies, or antigen-binding fragments thereof, of claim 48. 50. A kit for the diagnosis of pancreatic cancer comprising one or more of the nucleic acids coding for the marker of claims 26 to 28.

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51. A kit for screening of compounds that activate or inhibit any of the polypeptides listed in table 5 and/or 6, or stimulate or inhibit the expression of any of said polypeptides. The kit of claim 51, wherein said polypeptides are the polypeptides listed in table 6. 25.

53. The proteins, compounds, kits, methods and uses substantially as herein before described, especially with reference to the foregoing examples.

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SEQUENCE LISTING	Lys Gly Pro Val Ser Lys Tyr Ser Gln Ala Val Pro Ala Val Thr Glu
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<120> Specific Markers for Pancreatic Cancer	08 27 07 65
5 <130> 21525	5 Gly Glu 11e Gly 11e Gly Thr Pro Pro Gln Cys Phe Thr Val Val Phe
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	100 105 110
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10 <211> 412	10 115 120 125
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<213> Homo sapiens	130 135 140
. <220>	Gly Ser Leu Ser Gly Tyr Leu Ser Gln Asp Thr Val Ser Val Pro Cys
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15 <222> (1)(412)	15 Gln Ser Ala Ser Ala Ser Ala Leu Gly Gly Val Lys Val Glu Arg
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Met Gln Pro Ser Ser Leu Leu Pro Leu Ala Leu Cys Leu Leu Ala Ala	Ala Lys Phe Asp Gly Ile Leu Gly Met Ala Tyr Pro Arg Ile Ser Val
20 1 5 10 . 15	20 195 200 205
Pro Ala Ser Ala Leu Val Arg Ile Pro Leu His Lys Phe Thr Ser Ile	Asn Asn Val Leu Pro Val Phe Asp Asn Leu Met Gln Gln Lys Leu Val
20 25 30	210 215 220
Arg Arg Thr Met Ser Glu Val Gly Gly Ser Val Glu Asp Leu Ile Ala	Asp Gln Asn Ile Phe Ser Phe Tyr Leu Ser Arg Asp Pro Asp Ala Gln
35 40 45	225 230 235 240

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245 250 255		<211> 414	
Gly Ser Leu Ser Tyr Leu Asn Val Thr Arg Lys Ala Tyr Trp Gln Val		<212> PKT	,
260 265 270		<213> Homo sapiens	
5 His Leu Asp Gin Val Glu Val Ala Ser Gly Leu Thr Leu Cys Lys Glu		<220>	
275 280 . 285		<221> Isocitrate dehydrogenase [NADP] cytoplasmic	asmic
Gly Cys Glu Ale Ile Val Asp Thr Gly Thr Ser Leu Met Val Gly Pro		<222> (1)(414)	
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325 330 335		1 5 10	15
Ala ile Thr Leu Lys Leu Gly Gly Lys Gly Tyr Lys Leu Ser Pro Glu		Glu Met Thr Arg Ile Ile Trp Glu Leu Ile Lys Glu Lys Leu Ile Phe	lu Lys Leu Ile Phe
340 345 350		20 25	30
15 Asp Tyr Thr Leu Lys Val Ser Gln Ala Gly Lys Thr Leu Cys Leu Ser	51	Pro Tyr Val Glu Leu Asp Leu His Ser Tyr Asp Leu Gly Ile Glu Asn	eu Gly Ile Glu Asn
355 360 365		35 40	45
Gly Phe Met Gly Met Asp Ile Pro Pro Pro Ser Gly Pro Leu Trp Ile		Arg Asp Ala Thr Asn Asp Gin Val Thr Lys Asp Ala Ala Glu Ala Ile	la Ala Glu Ala Ile
370 375 380		50 55	. 09
Leu Gly Asp Val Phe Ile Gly Arg Tyr Tyr Thr Val Phe Asp Arg Asp		Lys Lys His Asn Val Gly Val Lys Cys Ala Thr Ile Thr Pro Asp Glu	le Thr Pro Asp Glu
20 385 390 395 400		65 70 75	
Asn Asn Arg Val Gly Phe Ala Glu Ala Ala Arg Leu		Lys Arg Val Glu Glu Phe Lys Leu Lys Gln Met Trp Lys Ser Pro Asn	rp Lys Ser Pro Asn
405 410	: -	85 90	56

Gly Thr Ile Arg Asn Ile Leu Gly Gly Thr Val Phe Arg Glu Ala Ile

11			
115 126 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127 127			
113		PCT/EP2003/014057	
116 116 Gly Arg His Ala Dy Gly Asp Glu Tyr Arg Ala Thr Asp Phe 110 115	Ile Cys Lys Asn Ile Pro Arg Leu Val	Ser Gly Trp Val Lys Pro Ile	ale Glu ale ale Hie Gly Thr Vel Thr arg His Tyr Arg Met Tyr Gln
130 130 131 132 130 131 130 131 130 131 130 131 130 131 130 131 130 131 130 131 130 131 130 131 130 131 130 131 130 131 130 131 130 131 130 131 130 130 131 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 1		125	310
130 135 140 135 140 145 140 145 140 145 140 145 140 145 140 145 140 145 140 145 140 145 140 145 140 145 140 145 140 145 140 145 140 145 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140	Ile Ile Gly Arg His Ala Tyr Gly Asp	Gln Tyr Arg Ala Thr Asp Phe	Lys Gly Gln Glu Thr Ser Thr Asn Pro 11e Ala Ser 11e Phe Ala Trp
145 146 147 148 149 149 149 141 149 141 149 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 141 1	130 135	140	
145 150 158 168 168 168 168 168 168 168 168 168 16	5 Val Val Pro Gly Pro Gly Lys Val Glu	lle Thr Tyr Thr Pro Ser Asp	5 Thr Arg Gly Leu Ala His Arg Ala Lys Leu Asp Asn Asn Lys Glu Leu
Gly the Glu Lys val The Tyr Lea val His Amm Phe Glu Glu Gly Gly 185 Gly Val Ala Met Gly Met Tyr Amn Gln Amp Lys Ser Ile Glu Amp Phe 180 Ala His Ser Ser Phe Gln Met Ala Lea Ser Lys Gly Trp Pro Leu Tyr 195 Amp Ile Phe Gln Clu Ile Tyr Amp Lys Gry Tyr Amp Gly Arg Phe Lys 210 215 220 Amp Ile Phe Gln Clu Ile Tyr Amp Lys Gly Tyr Lys Ser Gln Phe Glu 225 Amp Ile Phe Gln Clu Ile Tyr Amp Lys Gly Tyr Lys Ser Gln Phe Glu 226 Amp Gln Lys Ile Tyr Glu His Arg Leu Ile Amp Amp Met Val Ala 245 256 Amp Gly Amp Val Gln Ser Amp Ser Val Am Gly Tyr Gly Ser Leau 277 286 Amp Gly Amp Val Gln Ser Amp Ser Val Am Gly Tyr Gly Ser Leau 278 Gly Met Met Thr Ser Val Leu Val Cys Pro Amp Gly Lys Thr Val Glu 279 300 Amp Gly Met Met Thr Ser Val Leu Val Cys Pro Amp Gly Lys Thr Val Glu 279 300			340 345
155	Gly Thr Gln Lys Val Thr Tyr Leu Val	His Asn Phe Glu Glu Gly Gly	Ala Phe Phe Ala Asn Ala Leu Glu Glu Val Ser Ile Glu Thr Ile Glu
City Val Ala Met City Met Tyzt Ann Ciln Aap Lyus Ser Ile Cilu Aap Phe 180 Ala Met Cily Met Ala Leu Ser Ile Cilu Aap Phe 190 Ala Mis Ser Ser Phe Ciln Met Ala Leu Ser Lyus City Tyy Asp City Tyy Asp City Arg Phe Lyus 200 Ala Cilu Ile Tyy Asp Liu Lyus Aan Tht Ile Leu Lyus Lyus Tyyr Asp Cilu Phe Cilu Ala Cilu Ile Tyy Asp Lyus Cilu Phe Cilu Phe Cilu Cilu Ile Tyy Asp Lyus Cilu Phe Cilu Cilu Ile Tyy Asp Leu Ile Aap Aap Met Val Ala Cilu Ile Tyy Cilu His Arg Leu Ile Aap Aap Met Val Ala Cilu Ala Met Lyus Ser Cilu Cily Phe Ile Try Ala Cys Lyus Aan Tyyr 200 Ala Cilu Ala Met Lyus Ser Cilu Cily Phe Ile Try Ala Cilu Cily Aap Cilu Cilu Cilu Cilu Cilu Cilu Cilu Cilu			360
180 185 185 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190 190	Gly Val Ala Met Gly Met Tyr Asn Gln	Asp Lys Ser Ile Glu Asp Phe	Ala Gly Phe Met Thr Lys Asp Leu Ala Ala Cys Ile Lys Gly Leu Pro
Ala Hie Ser Ser Phe Gln Het Ala Leu Ser Lys Gly Trp Pro Leu Tyr 195 200 205 Leu Ser Thr Lys Asn Thr Ile Leu Lys Lys Tyr Asp Gly Arg Phe Lys 210 Asp Ile Phe Gln Glu Ile Tyr Asp Lys Gln Tyr Lys Ser Gln Phe Glu 225 Ala Gln Lys Ile Trp Tyr Glu His Arg Leu Ile Asp Asp Met Val Ala 245 245 Gln Ala Met Lys Ser Glu Gly Gly Phe Ile Trp Ala Cys Lys Asn Tyr 260 Asp Gly Asp Val Gln Ser Asp Ser Val Ala Gln Gly Tyr Gly Ser Leu 275 380 295 Gly Met Met Thr Ser Val Leu Val Cys Pro Asp Gly Lys Thr Val Glu 290 390 390	180	190	375 . 375
Leu Ser Thr Lys Asn Thr lie Leu Lys Lys Tyr Asp Gly Arg Phe Lys 210 215 210 Asp Ile Phe Glin Glu Ile Tyr Asp Lys Gln Tyr Lys Ser Glin Phe Glu 225 Ala Glin Lys Ile Trp Tyr Glu His Arg Leu Ile Asp Asp Met Val Ala 245 245 250 Ala Glin Lys Ile Trp Tyr Glu His Arg Leu Ile Asp Asp Met Val Ala 245 245 250 250 250 260 Asp Gly Asp Val Glin Gly Gly Phe Ile Trp Ala Gly Gly Ser Leu 260 265 270 Asp Gly Met Met Thr Ser Val Ala Glin Gly Tyr Gly Ser Leu 275 286 Gly Met Met Thr Ser Val Leu Val Cys Pro Asp Gly Lys Thr Val Glu 290 290	Ala His Ser Ser Phe Gln Met Ala Leu :	Ser Lys Gly Trp Pro Leu Tyr	Asn Val Gln Arg Ser Asp Tyr Leu Asn Thr Phe Glu Phe Met Asp Lys
Leu Ser Thr Lyss Asn Thr Ile Leu Lys Lys Tyr Asp Gly Arg Phe Lys 210 215 220 Asp Ile Phe Gln Glu Ile Tyr Asp Lys Gln Tyr Lys Ser Gln Phe Glu 225 236 Ala Gln Lys Ile Trp Tyr Glu His Arg Leu Ile Asp Asp Met Val Ala 245 246 240 Ala Gln Lys Ile Trp Tyr Glu His Arg Leu Ile Asp Asp Met Val Ala 245 250 250 Asp Gly Asp Val Gln Gly Gly Phe Ile Trp Ala Cys Lys Asn Tyr 260 265 270 Asp Gly Asp Val Gln Ser Asp Ser Val Ala Gln Gly Tyr Gly Ser Leu 275 280 285 Gly Met Thr Ser Val Leu Val Cys Pro Asp Gly Lys Thr Val Glu 290 290 290		205	390
210	Leu Ser Thr Lys Asn Thr Ile Leu Lys l	Lys Tyr Asp Gly Arg Phe Lys	heu Gly Glu Asn Leu Lys Ile Lys Leu Ala Gln Ala Lys Leu
Asp IIe Phe Glu Glu IIe Tyr Asp Lys Glu Phe Glu		220	
Ala Gln Lys Ile Trp Tyr Glu His Arg Leu Ile Asp Asp Met Val Ala 245 245 245 246 246 247 246 247 247 248 241 248 241 248 241 248 241 248 241 248 241 248 241 248 241 241		Gln Tyr Lys Ser Gln Phe Glu .	15.
Ala Glu Lys Ile Trp Tyr Glu His Arg Leu Ile Asp Asp Met Val Ala 245 250 255 Glu Ala Met Lys Ser Glu Gly Phe Ile Trp Ala Cys Lys Asn Tyr 260 260 265 Asp Gly Asp Val Gln Ser Asp Ser Val Ala Gln Gly Tyr Gly Ser Leu 275 275 Gly Met Met Thr Ser Val Leu Val Cys Pro Asp Gly Lys Thr Val Glu 290 290 290 290 295 300 295 300 295 300 295 300 295 300 295 300 295 300 295 300 295 300 295 300 295			
Clu Ala Met Lys Ser Glu Gly Gly Phe Ile Trp Ala Cys Lys Asn Tyr Clu Ala Met Lys Ser Glu Gly Phe Ile Trp Ala Cys Lys Asn Tyr 260 265 270 200 213> 270 213> 270 213> 270 213> 275 280 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285 285	Ala Gln Lys Ile Trp Tyr Glu His Arg l	Leu Ile Asp Asp Met Val Ala	
Gln Ala Met Ly8 Ser Glu Gly Gly Phe Ile Trp Ala Cy8 Ly8 Asn Tyr 260 265 270 Asp Gly Asp Val Gln Ser Asp Ser Val Ala Gln Gly Tyr Gly Ser Leu 275 278 278 Gly Met Thr Ser Val Leu Val Cy8 Pro Asp Gly Ly8 Thr Val Glu 290 290 201 202 202 203 203 203 203 20			
260 Asp Gly Asp Val Gln Ser Asp Ser Val Ala Gln Gly Tyr Gly Ser Leu 275 286 285 Gly Met Met Thr Ser Val Leu Val Cys Pro Asp Gly Lys Thr Val Glu 290 295 300	Gln Ala Met Lys Ser Glu Gly Gly Phe 1	Ile Trp Ala Cys Lys Asn Tyr	
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1 5 10 15	195 200 205
5 Ala Leu Cys Ala Leu Ser Leu Pro Val Arg Ala Ala Thr Ala Ser Arg	5 Ser Phe Asn Asn Gly Asp Cys Phe Ile Leu Asp Leu Gly Asn Asn Ile
20 25 30	210 215 220
Gly Ala Ser Gln Ala Gly Ala Pro Gln Gly Arg Val Pro Glu Ala Arg	His Gin Trp Cys Gly Ser Asn Ser Asn Arg Tyr Glu Arg Leu Lys Ala
35 40 45	225 230 235 240
Pro Asn Ser Met Val Val Glu His Pro Glu Phe Leu Lys Ala Gly Lys	Thr Gln Val Ser Lys Gly 11e Arg Asp Asn Glu Arg Ser Gly Arg Ala
56 60	. 10 245 250 255
Glu Pro Gly Leu Gln 11e Trp Arg Val Glu Lys Phe Asp Leu Val Pro	Arg Val His Val Ser Glu Glu Gly Thr Glu Pro Glu Ala Met Leu Gln
65 70 75 80	260 265 270
Val Pro Thr Asn Leu Tyr Gly Asp Phe Phe Thr Gly Asp Ala Tyr Val	Val Leu Gly Pro Lys Pro Ala Leu Pro Ala Gly Thr Glu Asp Thr Ala
95 06 58	275 280 285
ile Leu Lys Thr Val Gin Leu Arg Asn Gly Asn Leu Gin Tyr Asp Leu	15 Lys Glu Asp Ala Asn Arg Lys Leu Ala Lys Leu Tyr Lys Val Ser
100 105 110	290 295 300
His Tyr Trp Leu Gly Asn Glu Cys Ser Gln Asp Glu Ser Gly Ala Ala	Asn Gly Ala Gly Thr Met Ser Val Ser Leu Val Ala Asp Glu Asn Pro
115 120 125	305 310 315 320
Ala Ile Phe Thr Val Gln Leu Asp Asp Tyr Leu Asn Gly Arg Ala Val	Phe Ala Gln Gly Ala Leu Lys Ser Glu Asp Cys Phe Ile Leu Asp His
130 135 140	325 330 335
Gln His Arg Glu Val Gln Gly Phe Glu Ser Ala Thr Phe Leu Gly Tyr	Gly Lys Asp Gly Lys 11e Phe Val Trp Lys Gly Lys Gln Ala Asn Thr
145 150 155 160	340 345 350
Phe Lys Ser Gly Leu Lys Tyr Lys Lys Gly Gly Vai Ala Ser Gly Phe	Glu Glu Arg Lys Ala Ala Leu Lys Thr Ala Ser Asp Phe Ile Thr Lys
165 170 175	355 360

PCT/EP2003/014057	Ala Ser Thr Arg Leu Phe Gin Val Arg Ala Asn Ser Ala Gly Ala Thr	. 572	Arg Ala Val Glu Val Leu Pro Lys Ala Gly Ala Leu Asn Ser Asn Asp	. SBS	Ala Phe Val Leu Lys Thr Pro Ser Ala Ala Tyr Leu Trp Val Gly Thr	909 009	Gly Ala Ser Glu Ala Glu Lys Thr Gly Ala Gln Glu Leu Leu Arg Val	615 620	Leu Arg Ala Gin Pro Val Gin Val Ala Giu Gly Ser Giu Pro Asp Gly	630 635 640	Phe Trp Glu Ala Leu Gly Gly Lys Ala Ala Tyr Arg Thr Ser Pro Arg	950 059	Leu Iys Asp Lys Lys Met Asp Ala His Pro Pro Arg Leu Phe Ala Cys	665 670	Ser Asn Lys 11e Gly Arg Phe Val 11e Glu Glu Val Pro Gly Glu Leu	989 089	Met Gin Glu Asp Leu Ala Thr Asp Asp Vel Met Leu Leu Asp Thr Trp	. 695	Asp Gln Val Phe Val Trp Val Gly Lys Asp Ser Gln Glu Glu Glu Lys	710 715 720	Thr Glu Ala Leu Thr Ser Ala Lys Arg Tyr Ile Glu Thr Asp Pro Ala	730 735	Asn Arg Asg Arg Thr Pro 11e Thr Val Val Lys Gln Gly Phe Glu	
WO 2004/055519	Ala Ser Thr Arg Leu E	565	Arg Ala Val Glu Val I	085	5 Ala Phe Val Leu Lys T	565	Gly Ala Ser Glu Ala G	610	Leu Arg Ala Gln Pro V	10 · 625	Phe Trp Glu Ala Leu G	645	Leu Lys Asp Lys Lys N	099	15 Ser Asn Lys Ile Gly A		Met Gin Glu Asp Leu A	. 069	Asp Gin Val Phe Val I	20 705 7	Thr Glu Ala Leu Thr S	725	Asn Arg Asp Arg Arg T	•
PCT/EP2003/014057 9/335	Met Asp Tyr Pro Lys Gln Thr Gln Val Ser Val Leu Pro Glu Gly Gly	375 380	Glu Thr Pro Leu Phe Lys Gln Phe Phe Lys Asn Trp Arg Asp Pro Asp	390 395 400	Gln Thr Asp Gly Leu Gly Leu Ser Tyr Leu Ser Ser His Ile Ala Asn	410 415	Val Glu Arg Val Pro Phe Asp Ala Ala Thr Leu His Thr Ser Thr Ala	425 430	Met Ala Ala Gin His Gly Met Asp Asp Asp Gly Thr Gly Gin Lys Gin	440 . 445	ile Trp Arg ile Glu Gly Ser Asn Lys Val Pro Val Asp Pro Ala Thr	455 460	Tyr Gly Gln Phe Tyr Gly Gly Asp Ser Tyr Ile Ile Leu Tyr Asn Tyr	470 475 480	Arg His Gly Gly. Arg Gln Gly Gln Ile Ile Tyr Asn Trp Gln Gly Ala	490 495	Gln Ser Thr Gln Agp Glu Val Ala Ala Ser Ala Ile Leu Thr Ala Gln	510	Leu Asp Glu Glu Leu Gly Gly Thr Pro Val Gln Ser Arg Val Val Gln	520 525	Gly Lys Glu Pro Ala His Leu Met Ser Leu Phe Gly Gly Lys Pro Met	535 540	Ile Ile Tyr Lys Gly Gly Thr Ser Arg Glu Gly Gly Gln Thr Ala Pro	
WO 2004/055519	Met Asp Tyr Pro Lys G	370	Glu Thr Pro Leu Phe Ly	385 35	5 Gln Thr Asp Gly Leu Gl	405	Val Glu Arg Val Pro P!	420	Met Ala Ala Gln His Gl	10 435	Ile Trp Arg Ile Glu Gl	450	Tyr Gly Gln Phe Tyr Gl	465 47	15 Arg His Gly Gly Arg Gl	485	Gln Ser Thr Gln Asp Gl		Leu Asp Glu Glu Leu Gl	20 515	Gly Lya Glu Pro Ala Hi	. 530	lle lle Tyr Lys Gly Gl	

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Pro Pro Ser Phe Val Gly Trg	Pro Pro Ser Phe Val Gly Trp Phe Leu Gly Trp Asp Asp Asp Tyr Trp	Gly Phe Tyr Pro Tyr Pro Val Gln Thr Arg Thr Cys Arg Ser Thr Gly	hr Gly
755	760 765	65 70 75	
Ser Val Asp Pro Leu Asp Arç	Ser Val Asp Pro Leu Asp Arg Ala Met Ala Glu Leu Ala Ala	Ser Trp Ser Thr Leu Lys Thr Gln Asp Gln Lys Thr Val Ard Lys Ala	we Ala
377 077	780	6 06 58	95
	n ·	Glu Cys Arg Ala Ile His Cys Pro Arg Pro His Asp Phe Glu Asn Gly	ien Gly
		100 105	
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Met Gly Ser Asn Leu Ser Pro	Met Gly Ser Asn Leu Ser Pro Gln Leu Cys Leu Met Pro Phe Ile Leu	Arg 6ly Leu Thr Leu Arg 6ly Ser 6ln Arg Arg Thr Cys 6ln 6lu 6ly	1u 61y
1 5	10 15	200 205	
Gly Leu Leu Ser Gly Gly Val Thr Thr Thr Pro Tr	Thr Thr Thr Pro Trp Ser Leu Ala Arg	Gly Ser Trp Ser Gly Thr Glu Pro Ser Cys Gln Asp Ser Phe Met Tyr	et Tyr
20	25 30 20	210. 215 220	
Pro Gln Gly Ser Cys Ser Leu Glu Gly Val Glu Il	Glu Gly Val Glu Ile Lys Gly Gly Ser	Asp Thr Pro Gin Glu Val Ala Glu Ala Phe Leu Ser Ser Leu Thr Glu	hr Glu
35	40 45	225 230 235	240
Phe Arg Leu Leu Gln Glu Gly	Phe Arg Leu Leu Gln Glu Gly Gln Ala Leu Glu Tyr Val Cys Pro Ser	Thr lle Glu Gly Val Asp Ala Glu Asp Gly His Gly Pro Gly Glu Gln	lu Gln
50 55	09	245 250 25	. 255

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	Gln Lys Arg Lys Ile Val Leu Asp Pro Ser Gly Ser Met A	Met Asn Ile Tyr	Glu Gln His Val Phe Lys Val Lys Asp Met Glu Asn Leu Glu Asp Val
	260 265	. 270	450 455 460
	Leu Val Leu Asp Gly Ser Asp Ser Ile Gly Ala Ser Asn Phe Thr	Asn Phe Thr Gly	Phe Tyr Gln Met 11e Asp Glu Ser Gln Ser Leu Ser Leu Cys Gly Met
	275 280	285	465 470 475 480
ı,	Ala Lys Lys Cys Leu Val Asn Leu Ile Glu Lys Val Ala	Ala Ser Tyr Gly	5 Val Try Glu His Arg Lys Gly Thr Asp Tyr His Lys Gln Pro Try Gln
	290 295 300		485 490 495
	Val Lys Pro Arg Tyr Gly Leu Val Thr Tyr Ala Thr Tyr	Tyr Pro Lys 11e	Ala Lys Ile Ser Val Ile Arg Pro Ser Lys Gly His Glu Ser Cys Met
	305 310 315	320	500 505 510
	Trp Val Lys Val Ser Glu Ala Asp Ser Ser Aşn Ala Asp	Asp Trp Val Thr	Gly Ala Val Val Ser Glu Tyr Phe Val Leu Thr Ala Ala His Cys Phe
2	325 330	335	10 515 520 525
	Lys Gln Leu Asn Glu Ile Asn Tyr Glu Asp His Lys Leu Lys Ser Gly	Leu Lys Ser Gly	Thr Val Asp Asp Lys Glu His Ser Ile Lys Val Ser Val Gly Gly Glu
	340 345	350	530 535 540
	Thr Asn Thr Lys Lys Ala Leu Gln Ala Val Tyr Ser	Ser Met Met Ser Trp	Lys Arg Asp Leu Glu Ile Glu Val Val Leu Phe His Pro Asn Tyr Asn
	355 360	365	545 550 555 560
15	Pro Asp Asp Val Pro Pro Glu Gly Trp Asn Arg Thr Arg His Val Ile	Arg His Val Ile	15 Ile Asn Gly Lys Lys Glu Ala Gly Ile Pro Glu Phe Tyr Asp Tyr Asp
	370 375 380		565 570 575
	ile Leu Met Thr Asp Gly Leu His Asn Met Gly Gly Asp	Asp Pro 11e Thr	Val Ala Leu Ile Lys Leu Lys Asn Lys Leu Lys Tyr Gly Gln Thr Ile
	385 390 395	400	580 585 590
	Val Ile Asp Glu Ile Arg Asp Leu Leu Tyr Ile Gly Lys Asp Arg Lys	Гув Авр Агд Гув	Arg Pro 11e Cys Leu Pro Cys Thr Glu Gly Thr Thr Arg Ale Leu Arg
8	405 410	415	20 595 600 605
	Asn Pro Arg Glu Asp Tyr Leu Asp Val Tyr Val Phe Gly Val Gly Pro	Gly Val Gly Pro	Leu Pro Thr Thr Thr Cys Gln Gln Gln Lys Glu Glu Leu Leu Pro
	420 425	430	610 615 620
	Leu Val Asn Gln Val Asn Ile Asn Ala Leu Ala Ser Lys Lys Asp Asn	Lys Lys Asp Asn	Ala Gln Asp Ile Lys Ala Leu Phe Val Ser Glu Glu Lys Lys Leu
	435 440	445	625 630 635 640

Companience		
643 647 11e bye han Gly Nep Lye Gly Gls 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 670 655 650 655 670 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 650 655 655	. 15/335	
610 At 8 AD Ala Gln Tyr Ala Ero Gly Tyr And Lyva And Ilva And Illa 666 667 665 679 Ser Clu Val Val Thr Pro Arg Phe Leu Cya Thr Gly Gly Val Ser Pro 675 689 689 689 770 689 770 770 675 770 770 770 770 770 771 770 771 770 770 Fig Ala Arg Ser Arg Phe Ile Gln Val Gly Val Ile Ser Trp Gly 774 771 772 773 773 773 773 773 773 773 773 773	Thr Arg Lys Glu Val Tyr Ile Lys Asn Gly Asp Lys Lys Gly Ser Cys	
Ser Alw Asp Ale Cln Tyx Ale Pro Cly Tyx Asp Tyx Tyy	645 650 655	
Ser Glu Val Val Thr Fro Arg Rho Leu Cyg Thr Gly Gly Val Sar Pro 675 680 685 797 Ala Amp Pro Amn Thr Cyg Arg Gly Amp Ser Gly Gly Val Sar Pro 690 693 700 710 711 712 710 714 715 716 118 719 719 719 719 719 719 719	Glu Arg Asp Ala Gln Tyr Ala Pro Gly Tyr Asp Lys Val Lys Asp Ile	
Ser Glu val val Thr Fro Arg Phe Leu Cys Thr Gly Gly val Ser Pro 675 680 685 797 Ale Aug Pro Ann Thr Cya Arg Gly Ang Ser Gly Gly Pro Leu Ile 690 695 700 700 710 715 720 720 701 715 710 715 720 702 715 710 715 720 703 735 730 735 730 735 Fig. Ang Phe Hie Ile Ann Leu Phe Gln Val Leu Pro Ala 705 725 720 730 735 Fig. Ala Arg Ang Phe Hie Ile Ann Leu Phe Gln Val Leu Pro Trp Leu 707 740 745 760 708 Glu Lys Leu Gln Ang Glu Ang Leu Gly Phe Leu 709 750 760 710 751 760 721 755 760 722 750 760 723 PRT <		
757 Ala Amp Pro Amn Thi Cye Arg Gly Amp Ser Gly Gly Pro Leu Ille 630 635 700 700 701 702 710 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 711 711		
73x Ala Amp Pro Amn Thr Cym Arg Gly Amp Ser Gly Gly Pro Leu Ille 690 Val His Lym Arg Ser Arg Phe Ile Gln Val Gly Val Ile Ser Trp Gly 705 710 715 720 Val His Ala Val Cys Lym Amn Gln Lym Arg Gln Lym Gln Val Pro Ala 725 730 730 730 735 740 745 745 750 Lym Glu Lyg Leu Gln Amp Glu Amp Leu Phe Gln Val Leu 745 750 Lym Glu Lyg Leu Gln Amp Glu Amp Leu Gly Phe Leu 750 135 760 135 760 137 738 740 741 745 750 138 740 745 750 139 740 741 750 750 750 750 750 750 750 75	680	5 10
450 655 700	Tyr Ala Asp Pro Asn Thr Cys Arg Gly Asp Ser Gly Gly Pro Leu Ile	Ser Ale Gly Asn Gly Ale Gly Gly Gly Ser Met Gly Asp Tyr Net
Val His Lys Arg Ser Arg Phe Ile Gin Val Gly Val Ile Ser Trp Gly 705 710 715 720 720 720 720 721 725 730 735 740 745 750 Lys Gin Lys Leu Gin Asp Leu Phe Gin Val Leu Pro Trp Leu 740 745 750 Lys Giu Lys Leu Gin Asp Leu Gly Phe Leu 750 Lys Giu Lys Leu Gin Asp Leu Gly Phe Leu 751 752 750 Lys Giu Lys Leu Gin Asp Leu Gly Phe Leu 751 752 750 Lys Giu Lys Leu Gin Asp Leu Giy Phe Leu 751 752 750 Lys Giu Lys Leu Gin Asp Leu Giy Phe Leu 750 750 Lys Giu Lys Leu Gin Asp Leu Giy Phe Leu 750 750 Lys Giu Lys Leu Gin Asp Leu Giy Phe Leu 750 750 750 C211> 750 750 750 C212> 750 C221> 750 C221 750 C221 750 C221 75	695	20 25 30
110 715 720 720 720 720 720 720 720 720 720 725 730 735 735 730 735 735 730 735 735 740 745 745 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750 750	Val His Lys Arg Ser Arg Phe ile Gln Val Gly Val ile Ser Trp Gly	Ala Gln Glu Asp Asp Trp Asp Arg Asp Leu Leu Leu Asp Pro Ala Trp
Val Val Amp Val Cys Lys Amn Gln Lys Arg Gln Val Pro Ala 725 730 735 His Ala Arg Amp Phe His Ile Amn Leu Phe Gln Val Leu Pro Trp Leu 740 745 750 Lys Glu Lys Leu Gln Amp Glu Amp Leu Gly Phe Leu 755 750 2210> 5 2211> PRT 2221> Homo sapiens 4220> 2221> Alpha-actinin 4	705 710 715	35 40
His Ala Arg Asp Phe His Ile Asn Leu Phe Gln Val Leu Pro Try Leu 740 745 750 Lys Glu Lys Leu Gln Asp Glu Asp Leu Gly Phe Leu 755 <210> 5 <211> PRT <211> PRT <221> PRT <220> <220> <221> Alpha-actinin 4	Val Val Asp Val Cys Lys Asn Gln Lys Arg Gln Lys Gln Val Pro Ala	Glu Lys Gln Gln Arg Lys Thr Phe Thr Ala Trp Cys Asn Ser His Leu
His Ala Arg Asp Phe His Ile Asn Leu Phe Gln Val Leu Pro Trp Leu 140 745 750 Lys Glu Lys Leu Gln Asp Glu Asp Leu Gly Phe Leu 755 760 <210> 5 <211> 911 <212> PRT <213> PRT <213> Alpha-actinin 4	730	09 55 05
Lys Glu Lys Leu Gln Asp Glu Asp Leu Gln Asp Deu Gly Phe Leu 750 Lys Leu Gln Asp Glu Asp Leu Gly Phe Leu 760 <210> 5 <211> 911 <212> PRT <2213> Homo sapiens <220> Alpha-actinin 4	His Ala Arg Asp Phe His Ile Asn Leu Phe Gln Val Leu Pro Trp Leu	Arg Lys Ala Gly Thr Gln Ile Glu Asn Ile Asp Glu Asp Phe Arg Asp
Lys Glu Lys Leu Gln Asp Glu Asp Leu Gly Phe Leu -210> 5 -211> 911 -212> PRT -213> Homo sapiens -220> -221> Alpha-actinin 4	740 . 745	27 07
755 760 <210> 5 <211> PRT <212 PRT <213 Homo sapiens <220> <220> <221> Alpha-actinin 4		15 Gly Leu Lys Leu Met Leu Leu Glu Val Ile Ser Gly Glu Arg Leu
<pre><210> 5 <211> 911 <212> PRT <213> Homo sapiens <220> <220> <221> Alpha-actinin 4</pre>		56 06 58
<pre><210> 5 <211> 911 <212> PRT <213> Homo sapiens <220> <221> Alpha-actinin 4</pre>		Pro Lys Pro Glu Arg Gly Lys Met Arg Val His Lys Ile Asn Asn Val
<pre><210> 5 <211> 911 <212> PRT <213> Homo sapiens <220> <221> Alpha-actinin 4</pre>		105
<pre><211> 911 <212> PHT <213> Home sapiens <220> <221> Alpha-actinin 4</pre>		
Homo sapiens Alpha-actinin 4	<211>	115
Homo sapiens Met Ile Trp Thr Ile Ile Leu Arg Phe Ala Ile Gln Asp Ile Ser Alpha-actinin 4 145 150 155	<212> PRT	ile Gly Ala Glu Glu Ile Val Asp Gly Asn Ala Lys Met Thr Leu Gly
Alpha-actinin 4 155 155 155	<213> Homo sapiens	135
145 150 155	<220>	Met ile Trp Thr ile lie Leu Arg Phe Ala ile Gln Asp ile Ser Val
	<221> Alpha-actinin 4	150 155

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Glu Glu Thr Ser Ala Lys Glu Gly Leu Leu Leu Trp Cys Gln Arg Lys	Leu Glu Ile Asn Phe Asn Thr Leu Gln Thr Lys Leu Arg Leu Ser Asn
165 170 175	355 360 365
Thr Ale Pro Tyr Lys Asn Val Asn Val Gln Asn Phe His Ile Ser Trp	Arg Pro Ala Phe Met Pro Ser Glu Gly Lys Met Val Ser Asp Ile Asn
180 185 190	370 375 380
5 Lys Asp Gly Leu Ala Phe Asn Ala Leu Ile His Arg His Arg Pro Glu	5 Asn Gly Trp Gln His Leu Glu Gln Ala Glu Lys Gly Tyr Glu Glu Trp
. 200 205	385 390 395 400
Leu Ile Glu Tyr Asp Lys Leu Arg Lys Asp Asp Pro Val Thr Asn Leu	Leu Leu Asn Glu Ile Arg Arg Leu Glu Arg Leu Asp His Leu Ala Glu
210 215 220	405 410 415
Asn Asn Ale Phe Glu Val Ala Glu Lys Tyr Leu Asp Ile Pro Lys Met	Lys Phe Arg Gln Lys Ala Ser Ile His Glu Ala Trp Thr Asp Gly Lys
10 225 230 235 240	10 420 425 430
Leu Asp Ala Glu Asp Ile Val Asn Thr Ala Arg Pro Asp Glu Lys Ala	Glu Ala Met Leu Lys His Arg Asp Tyr Glu Thr Ala Thr Leu Ser Asp
245 250 255	435 440 445
Ile Met Thr Tyr Val Ser Ser Phe Tyr His Ala Phe Ser Gly Ala Gin	ile Lys Ala Leu ile Arg Lys His Glu Ala Phe Glu Ser Asp Leu Ala
260 265 270	450 455 460
15 Lys Ala Glu Thr Ala Ala Asn Arg Ile Cys Lys Val Leu Ala Val Asn	15 Ala His Gin Asp Arg Val Glu Gin Ile Ala Ala Ile Ala Gin Glu Leu
275 280 285	465 470 475 480
Gln Glu Aen Glu His Leu Met Glu Asp Tyr Glu Lys Leu Ala Ser Asp	Asn Glu Leu Asp Tyr Asp Ser His Asn Val Asn Thr Arg Cys Gln
290 295 300	485 490 495
Leu Leu Glu Trp Ile Arg Arg Thr Ile Pro Trp Leu Glu Asp Arg Val	Lys Ile Cys Asp Gln Trp Asp Ala Leu Gly Ser Leu Thr His Ser Arg
20 305 310 315 320	20 500 505 510 .
Pro Gln Lys Thr Ile Gln Glu Met Gln Gln Lys Leu Glu Asp Phe Arg	Arg Glu Ala Leu Glu Lys Thr Glu Lys Gln Leu Glu Ala 11e Asp Gln
325 330 335	515 520 525
Asp Tyr Arg Arg Val His Lys Pro Pro Lys Val Gln Glu Lys Cys Gln	Leu His Leu Glu Tyr Ala Lys Arg Ala Ala Pro Phe Asn Asn Trp Met
340 345 350	530 535 540

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		19/335			,	20/335	*10/5007 17/10 1
	Glu Ser Ala Met Glu Asp Leu Gln Asp Met Phe Il	u Gin Asp Met Phe ile Val	l His Thr Ile	. Glu G	ln beu beu Thr Thr	Glu Gln Leu Leu Thr Thr Ile Ala Arg Thr Ile Asn Glu Val Glu Asn	an Glu Val Glu Asn
	550	. 555	260		740	745	7.50
	Glu Glu Ile Glu Gly Leu Ile Ser Ala His Asp Gl	e Ser Ala His Asp Gln Phe	n Phe Lys Ser Thr	Gln	le Leu Thr Arg Asp	Gln lle Leu Thr Arg Asp Ala Lys Gly Ile Ser Gln Glu Gln Met Gln	iln Glu Gln Met Gln
	565	570	575	٠. ٠	755	760	765
ç	Leu Pro Asp Ala Asp Arg Glu Arg Glu Ala Ile Leu Ala Ile His Lys	u Arg Glu Ala Ile Leu Ale	Ile His Lys	5 Glu B	he Arg Ala Ser Phe	Glu Phe Arg Ala Ser Phe Asn His Phe Asp Lys Asp His Gly Gly Ala	sp His Gly Gly Ala
	580	585	290		7.00	775	780
	Glu Ala Gln Arg Ile Ala Glu Ser Asn His Ile Lys		Leu Ser Gly Ser	ren G	ily Pro Glu Glu Phe	Leu Gly Pro Glu Glu Phe Lys Ala Cys Leu Ile Ser Leu Gly Tyr Asp	er Leu Gly Tyr Asp
	595	600 605		785	790	795	. 008
	Asn Pro Tyr Thr Thr Val Thr Pro Gln Ile Ile Asn	r Pro Gln Ile Ile Asn Ser	: bys Trp Glu	Val G	ilu Asn Asp Arg Gln	Val Glu Asn Asp Arg Gln Gly Glu Ala Glu Phe Asn Arg Ile Met	sn Arg Ile Met Ser
91	610 615	5 620		10	808	810	815
	Lys Val Gln Gln Leu Val Pro Lys Arg Asp His Ala	_	Leu Glu Glu	Leu V	7al Asp Pro Asn His	Leu Val Amp Pro Amn Him Ser Gly Leu Val Thr Phe Gln Alm Phe	he Gln Ala Phe Ile
	625 630	635	640	•	820	825	830
	Gln Ser Lys Gln Gln Ser Asn Glu His Leu Arg Arg	_	Gln Phe Ala Ser	. Asp	the Met Ser Arg Glu	Asp Phe Met Ser Arg Glu Thr Thr Asp Thr Asp Thr Ala Asp Gln Val	thr Ala Asp Gln Val
	645	650	655		835	. 840	845
15	Gln Ala Asn Val Val Gly Pro Trp Ile Gln Thr Lys		Met Glu Glu Ile	15 Ile 2	la Ser Phe Lys Val	ile Ala Ser Phe Lys Val Leu Ala Gly Asp Lys Asn Phe Ile Thr Ala	wan Phe Ile Thr Ala
	099	665	670	w	850	855	860
	Gly Arg Ile Ser Ile Glu Met Asn Gly Thr Leu Glu		Asp Gln Leu Ser) ala	3lu Leu Arg Arg Glu	Glu Glu Leu Arg Arg Glu Leu Pro Pro Asp Gln Ala Glu Tyr Cys Ile	ala Glu Tyr Cye Ile
	. 675	680 685		865	870	875	088
	His Leu Lys Gln Tyr Glu Arg Ser Ile Val Asp Tyr		Lys Pro Asn Leu	Ala 7	Arg Met Ala Pro Tyr	Ala Arg Met Ala Pro Tyr Gln Gly Pro Asp Ala Val Pro Gly Ala Leu	/al Pro Gly Ala Leu
20	699 069	2 700		20	888	068	895
	Asp Leu Leu Glu Gln Gln His Gln Leu Ile Gln Glu		Ala Leu Ile Phe	Asp 1	lyr Lys Ser Phe Ser	Asp Tyr Lys Ser Phe Ser Thr Ala Leu Tyr Gly Glu Ser Asp Leu	slu Ser Asp Leu
	705 710	715	720		006	506	910
	Asp Asn Lys His Thr Asn Tyr Thr Met Glu His Ile		Arg Val Gly Trp	•			
	725	730	735				

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	<210> 6	Val Gly Ser Thr Thr Cln Leu Tyr Thr. Asp Arg Thr Glu Lys Leu	
	<211> 683	115 120 125	
	<212> PRT	Arg Pro Glu Met Glu Gly Pro Gly Ser Phe Thr Ile Phe Ala Pro Ser	
	<213> Homo sapiens	130 135 140	,
	5 <220>	5 Asn Glu Ala Trp Ala Ser Leu Pro Ala Glu Val Leu Asp Ser Leu Val	
	<221> Transforming growth factor-beta induced protein IG-H3 precursor	145 150 155 160	
-	<222> (1)(683)	Ser Asn Val Asn Ile Glu Leu Leu Asn Ala Leu Arg Tyr His Met Val	
-	<223> Accession No. as of 06 Dec 2002: Q15582	165 170 175	
	<400> <	Gly Arg Arg Val Leu Thr Asp Glu.Leu Lys His Gly Met Thr Leu Thr	
	01	10 180 185 190	
	Met Ala Leu Phe Val Arg Leu Leu Ala Leu Ala Leu Ala Leu	Ser Met Tyr Gln Asn Ser Asn Ile Gln Ile His His Tyr Pro Asn Gly	
· .	1 5 10 15	195 200 205	
	Gly Pro Ala Ala Thr Leu Ala Gly Pro Ala Lys Ser Pro Tyr Gln Leu	Ile Val Thr Val Asn Cys Ala Arg Leu Leu Lys Ala Asp His His Ala	
	20 25 30	210 215 220	
	15 Val Leu Gln His Ser Arg Leu Arg Gly Arg Gln His Gly Pro Asn Val	15 Thr Asn Gly Val Val His Leu Ile Asp Lys Val Ile Ser Thr Ile Thr	
	35 . 40 45	225 230 235 240	
	Cys Ala Val Gln Lys Val Ile Gly Thr Asn Arg Lys Tyr Phe Thr Asn	Asn Asn Ile Gln Gln Ile Ile Glu Ile Glu Asp Thr Phe Glu Thr Leu	
	50 55 60	245 250 255	
	Cys Lys Gln Trp Tyr Gln Arg Lys Ile Cys Gly Lys Ser Thr Val Ile	Arg Ala Ala Val Ala Ala Ser Gly Leu Asn Thr Met Leu Glu Gly Asn	
	20 65 70 75 80	20 260 265 270	
	Ser Tyr Glu Cys Cys Pro Gly Tyr Glu Lys Val Pro Gly Glu Lys Gly	Gly Gln Tyr Thr Leu Leu Ala Pro Thr Asn Glu Ala Phe Glu Lys Ile	
		275 280 285	
	Cys Pro Ala Ala Leu Pro Leu Ser Asn Leu Tyr Glu Thr Leu Gly Val	Pro Ser Glu Thr Leu Asn Arg Ile Leu Gly Asp Pro Glu Ala Leu Arg	
	100 105 110	290 295 300	
. ·			

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Asp Leu Leu Af	Asp Leu Leu Asn Asn His Ile Leu Lys Ser Ala Met Cys Ala Glu Ala	Ala Val Leu Thr Pro Pro Met Gly Thr Val Met Asp Val Leu Lys Gly Asp
305	310 315	320 505 510
ile Val Ala Gl	ile Val Ala Gly Leu Ser Val Glu Thr Leu Glu Gly Thr Thr Leu Glu	Glu
	325 . 330 . 335	515 520 525
5 Val Gly Cys Se	Val Gly Cys Ser Gly Asp Met Leu Thr Ile Asn Gly Lys Ala Ile Ile	Ile 5. Glu Thr Leu Asn Arg Glu Gly Val Tyr Thr Val Phe Ala Pro Thr Asn
340	345 350	530 535 540
Ser Asn Lys As	Ser Asn Lys Asp lle Leu Ala Thr Asn Gly Val lle His Tyr lle Asp	Asp
355	360 365	545 550 555 560
Glu beu beu Il	Glu Leu Leu Ile Pro Asp Ser Ala Lys Thr Leu Phe Glu Leu Ala Ala	Ala Ala Lys Glu Leu Ala Asn Ile Leu Lys Tyr His Ile Gly Asp Glu
10 370	375 380	10 565 570 575
Glu Ser Asp Va	Glu Ser Asp Val Ser Thr Ala Ile Asp Leu Phe Arg Gln Ala Gly Leu	Leu
385	390 395	280 585 590
Gly Asn His Le	Gly Asn His Leu Ser Gly Ser Glu Arg Leu Thr Leu Leu Ala Pro Leu	Leu
	405 410 415	509 009 555
15 Asn Ser Val Pho	Asn Ser Val Phe Lys Asp Gly Thr Pro Pro Ile Asp Ala His Thr Arg	Arg
420	0 425 430	610 615 620
Asn Leu Leu Ar	Asn Leu Leu Arg Asn His Ile Ile Lys Asp Gin Leu Ala Ser Lys Tyr	Tyr
435	440	625 630 635 640
Leu Tyr His Gl	Leu Tyr His Gly Gln Thr Leu Glu Thr Leu Gly Gly Lys Lys Leu Arg	Arg Glu Arg Gly Asp Glu Leu Ala Asp Ser Ala Leu Glu Ile Phe Lys Gln
20 450	455 460	20 645 650 655
Val Phe Val Ty.	Val Phe Val Tyr Arg Asn Ser Leu Cys Ile Glu Asn Ser Cys Ile Ala	Ala Ala Ser Ala Phe Ser Arg Ala Ser Cln Arg Ser Val Arg Leu Ala Pro
465	470 475	660 665 670
Ala His Asp Ly	Ala His Asp Lys Arg Gly Arg Tyr Gly Thr Leu Phe Thr Met Asp Arg	Arg Val Tyr Gln Lys Leu Leu Glu Arg Met Lys His
	485 490 495	675 680

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			Leu Asp Phe 11e Ala Ser Lys Gly Val Lys Leu Val Ser 11e Gly Ala	1 Val Ser Ile Gly Ala
			100 105	110
<210> 7			Glu Glu Ile Val Asp Gly Asn Val Lys Wet Thr Leu Gly Met Ile Trp	. Leu Gly Met Ile Trp
<211> 892			115 120	125
5 <212> PRT			5 Thr Ile Ile Leu Arg Phe Ala Ile Gln Asp Ile Ser Vel Glu Glu Thr	Ser Val Glu Glu Thr
<213> Homo sapiens	sapiens		130 135	140
<220>			Ser Ala Lys Glu Gly Leu Leu Leu Trp Cys Gln Arg Lys Thr Ala Pro	Arg Lys Thr Ala Pro
<221> Alpha-actinin 1	1-actinin 1		145 150 155	.160
<222> (1)	(1)(892)		Tyr Lys Aen Val Aen Ile Gln Aen Phe His Ile Ser Trp Lys Asp Gly	Ser Trp Lys Asp Gly
10 <223> Acces	<223> Accession No. P12814		10 165 170	175
<400> 7			Leu Gly Phe Cys Ala Leu Ile His Arg His Arg Pro Glu Leu Ile Asp	Pro Glu Leu Ile Asp
			180 185	190
Met Asp His	Met Asp His Tyr Asp Ser Gln Gln Thr Asn Asp Tyr Met Gln Pro Glu	ro Glu	Tyr Gly Lys Leu Arg Lys Asp Asp Pro Leu Thr Asn Leu Asn Thr Ala	. Asn Leu Asn Thr Ala
Ħ	5 10		195 200	205
15 Glu Asp Trp	Glu Asp Trp Asp Arg Asp Leu Leu Leu Asp Pro Ala Trp Glu I	Glu Lýs Gln	15 Phe Asp Val Ala Glu Lys Tyr Leu Asp Ile Pro Lys Met Leu Asp Ala	Lys Met Leu Asp Ala
	20 25 30		210 215	220
. Gln Arg Lys	Gln Arg Lys Thr Phe Thr Ala Trp Cys Asn Ser His Leu Arg Lys Ala	ys Ala	Glu Asp Ile Val Gly Thr Ala Arg Pro Asp Glu Lys Ala Ile Met Thr	Lys Ala Ile Met Thr
35	40 45		225 230 235	240
Gly Thr Gln	Gly Thr Gln Ile Glu Asn Ile Glu Glu Asp Phe Arg Asp Gly Leu Lys	eu Lys	Tyr Val Ser Ser Phe Tyr His Ala Phe Ser Gly Ala Gln Lys Ala Glu	Ala Gln Lys Ala Glu
20 50	55 60	2	20 245 250	255
Leu Met Leu	Leu Met Leu Leu Leu Glu Val Ile Ser Gly Glu Arg Leu Ala Lys Pro		Thr Ala Ala Asn Arg Ile Cys Lys Val Leu Ala Val Asn Gln Glu Asn	Val Asn Gln Glu Asn
65	70 75	80	260 . 265	. 270
Glu Arg Gly	Glu Arg Gly Lys Met Arg Val His Lys Ile Ser Asn Val Asn Lys Ala	ys Ala	Glu Gln Leu Met Glu Asp Tyr Glu Lys Leu Ala Ser Asp Leu Leu Glu	Ser Asp Leu Leu Glu
	5 06 58	95	275 280	285

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Trp lle Arg Arg Thr lle Pro Trp Leu Glu Asn Arg Val Pro Glu	Glu Asn Asp Asn Leu G	Asp Gin Trp Asp Asn Leu Gly Ala Leu Thr Gin Lys Arg Arg Glu Ala
290 295 300	485	490
Thr Met His Ala Met Gln Gln Lys Leu Glu Asp Phe Arg Asp Tyr	Tyr Arg	Leu Glu Arg Thr Glu Lys Leu Leu Glu Thr Ile Asp Gln Leu Tyr Leu
305 310 315	320 500	505 510
5 Arg Leu His Lys Pro Pro Lys Val Gin Glu Lys Cys Gin Leu Glu	Glu ile 5 Glu Tyr Ala Lyg Arg Ala Al	Glu Tyr Ala Lys Arg Ala Ala Pro Phe Asn Asn Trp Wet Glu Gly Ala
325 330 335	515	520 525
Asn Phe Asn Thr Leu Gln Thr Lys Leu Arg Leu Ser Asn Arg Pro	Pro Ala	Met Glu Asp Leu Gln Asp Thr Phe Ile Val His Thr Ile Glu Glu Ile
340 345 350	25 065	535 . 540
Met Val Ser Asp Ile Asn Asn	Ala Trp Gln Gly Leu Thr Thr Ala Hi	Gln Gly Leu Thr Thr Ala His Glu Gln Phe Lys Ala Thr Leu Pro Asp
10 355 360 365	10 545 550	955 558
Gly Cys Leu Glu Gln Val Glu Lys Gly Tyr Glu Glu Trp Leu Leu	Leu Asn Arg Leu Ala Asp Lys Glu Arg Leu Al	Ala Asp Lys Glu Arg Leu Ala Ile Leu Gly Ile His Asn Glu Val Ser
370 375 380	595	570 575
Glu Ile Arg Arg Leu Glu Arg Leu Asp His Leu Ala Glu Lys Phe	Phe Arg	Lys lle Val Gln Thr Tyr His Val Asn Met Ala Gly Thr Asn Pro Tyr
385 390 395	400	. 585
Gin Lys Ale Ser Ile His Glu Ale Trp Thr Asp Gly Lys Glu Ale	Ala Met	Thr Thr Ile Thr Pro Gln Glu Ile Asn Gly Lys Trp Asp His Val Arg
405 . 410 415	, \$85	909 009
Leu Arg Gln Lys Asp Tyr Glu Thr Ala Thr Leu Ser Glu Ile Lys	Lys Ala Gln Leu Val Pro Arg Arg As	Gin Leu Val Pro Arg Arg Asp Gin Ala Leu Thr Glu Glu His Ala Arg
420 425 430	610 615	.5 . 620
Leu Leu Lys Lys His Glu Ala Phe Glu Ser Asp Leu Ala Ala His	Gln Glu Ser Ve	Gln Gln His Asn Glu Ser Val Arg Lys Gln Phe Gly Ala Gln Ala Asn
20 435 440 445	20 625 . 630	635 640
Asp Arg Val Glu Gln Ile Ala Ala Ile Ala Gln Glu Leu Asn Glu Leu		Val Ile Gly Pro Trp lle Gln Thr Lys Met Glu Glu Ile Gly Arg Ile
450 455 460	645	650 655
Asp Tyr Tyr Asp Ser Pro Ser Val Asn Ala Arg Cys Gln Lys Ile Cys		Ser Ile Glu Met His Gly Thr Leu Glu Asp Gin Leu Ser His Leu Arg
465 470 475	480	665 670

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29/335 Glu fivr Glu Ivs Ser Ile Val Asn Tvr Ivs Pro Ivs Ile Asp Glu Leu	Sul335 Ala Pro Tyr Thr Gly Pro Asp Ser Val Pro Gly Ala Leu Asp Tyr Met
500 110 Act 014 0 F 014 0 F 104 105 100 100 0 F 110 0 F 110	
675 680 685	865 870 875 880
Glu Gly Asp His Gln Leu Ile Gln Glu Ala Leu Ile Phe Asp Asn Lys	Ser Phe Ser Thr Ala Leu Tyr Gly Glu Ser Asp Leu
690 695 700	885 890
5 His Thr Asn Tyr Thr Met Glu His Ile Arg Val Gly Trp Glu Gln Leu	vo
705 710 715 720	
Leu Thr Thr Ile Ala Arg Thr Ile Asn Glu Val Glu Asn Gln Ile Leu	<210> 8
725 730 735	<211> 448
Thr Arg Asp Ala Lys Gly Ile Ser Gln Glu Gln Met Asn Glu Phe Arg	<212> PRT
10 740 745 750	10 <213> Homo sapiens
Ala Ser Phe Asn His Phe Asp Arg Asp His Ser Gly Thr Leu Gly Pro	<220>
755 760 765	<221> Tubulin alpha-4 chain
Glu Glu Phe Lys Ala Cys Leu Ile Ser Leu Gly Tyr Asp Ile Gly Asn	<222> (1)(448)
770 775 780	<223> Accession No. P05215
15 Asp Pro Gln Gly Glu Ala Glu Phe Ala Arg Ile Met Ser Ile Val Asp	15 <400> 8
785 799 795 800	
Pro Asn Arg Leu Gly Val Val Thr Phe Gln Ala Phe Ile Asp Phe Met	Met Arg Glu Cys Ile Ser Val His Val Gly Gln Ala Gly Val Gln Met
805 810 815	1 , 5 10 15
Ser Arg Glu Thr Ala Asp Thr Asp Thr Ala Asp Gln Val Met Ala Ser	Gly Asn Ala Cys Trp Glu Leu Tyr Cys Leu Glu His Gly Ile Gln Pro
20 820 825 830	20 20 25 30
Phe Lys lle Leu Ala Gly Asp Lys Asn Tyr lle Thr Met Asp Glu Leu	Asp Gly Gln Met Pro Ser Asp Lys Thr Ile Gly Gly Gly Asp Asp Ser
835 840 845	35 40 45
Arg Arg Glu Leu Pro Pro Asp Gln Ala Glu Tyr Cys Ile Ala Arg Met	Phe Thr Thr Phe Phe Cys Glu Thr Gly Ala Gly Lys His Val Pro Arg
	. 09 25 09

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Ala Val Phe Val Asp Leu Glu Pro Thr Val Ile Asp Glu Ile Arg Asn	Thr Asn Leu Val Pro Tyr Pro Arg 11e His Phe Pro Leu Ala Thr Tyr
65 70 75 80	260 265 270
Gly Pro Tyr Arg Gln Leu Phe His Pro Glu Gln Leu Ile Thr Gly Lys	Ala Pro Val Ile Ser Ala Glu Lys Ala Tyr His Glu Gln Leu Ser Val
	275 280 285
5 Glu Asp Ala Ala Asn Tyr Ala Arg Gly His Tyr Thr Ile Gly Lys	5 Ala Glu Ile Thr Asn Ala Cys Phe Glu Pro Ala Asn Gln Met Val Lys
100 105 110	290 295 300
Glu Ile Ile Asp Pro Val Leu Asp Arg Ile Arg Lys Leu Ser Asp Gln	Cys Asp Pro Arg His Gly Lys Tyr Wet Ala Cys Cys Leu Leu Tyr Arg
115 120 125	305 310 315 320
Cys Thr Gly Leu Gin Gly Phe Leu Val Phe His Ser Phe Gly Gly	Gly Asp Val Val Pro Lys Asp Val Asn Ala Ala Ile Ala Ala Ile Lys
10 130 135 140	10 325 330 335
Thr Gly Ser Gly Phe Thr Ser Leu Leu Met Glu Arg Leu Ser Val Asp	Thr Lys Arg Ser Ile Gin Phe Val Asp Trp Cys Pro Thr Gly Phe Lys
145 150 155 160	340 345 350
Tyr Gly Lys Lys Ser Lys Leu Glu Phe Ser Ile Tyr Pro Ala Pro Gln	Val Gly lle Asn Tyr Gln Pro Pro Thr Val Val Pro Gly Gly Asp Leu
165 170 175	355 360 365
15 Val Ser Thr Ala Val Val Glu Pro Tyr Aen Ser Ile Leu Thr Thr His	is Ala Lys Val Gin Arg Ala Val Cys Met Leu Ser Asn Thr Thr Ala Ile
. 180 185 190	370 375 380
Thr Thr Leu Glu His Ser Asp Cys Ala Phe Met Val Asp Asn Glu Ala	Ala Glu Ala Trp Ala Arg Leu Asp His Lys Phe Asp Leu Met Tyr Ala
195 200 . 205	385 390 395 400
ile Tyr Asp ile Cys Arg Arg Asn Leu Asp ile Glu Arg Pro Thr Tyr	Lys Arg Ala Phe Val His Trp Tyr Val Gly Glu Gly Met Glu Gly
20 210 215 . 220	20 405 410 415
Thr Asn Leu Asn Arg Leu 11e Ser Gln 11e Val Ser Ser 11e Thr Ala	Glu Phe Ser Glu Ala Arg Glu Asp Met Ala Ala Leu Glu Lys Asp Tyr
225 230 235 240	420 425 430
Ser Leu Arg Phe Asp Gly Ala Leu Asn Val Asp Leu Thr Glu Phe Gln	Glu Glu Val Gly 11e Asp Ser Tyr Glu Asp Glu Asp Glu Gly Glu Glu
245 250 255	435 440 445

PCT/EP2003/014057 WO 2004/055519 34/335	Pro Thr Phe Arg Gln Met Gln Leu Glu Asn Val Ser Val Ala Leu Glu	100	Phe Leu Asp Arg Glu Ser Ile Lys Leu Val Ser Ile Asp Ser Lys Ala	115 120	5 Ile Val Asp Gly Asn Leu Lys Leu Ile Leu Gly Leu Ile Trp Thr Leu	130 135 140	. Ile Leu His Tyr Ser Ile Ser Met Pro Met Trp Asp Glu Glu Glu Asp	145 150 155	Glu Glu Ala Lys Lys Glu Thr Pro Lys Gln Arg Leu Leu Gly Trp Ile	10 165 170	Gln Asn Lys Leu Pro Gln Leu Pro 11e Thr Asn Phe Ser Arg Asp Trp	185	Gly Ala Ala Leu Gly Ala Leu Gly Ala Leu Gly Ala Leu Val Asp Ser Cys Ala Pro Gly	15 195 200	Ala Thr Glu	30 215 220	Gln Asn Thr . Ala Arg Glu Ala Met Gln Gln Ala Asp Asp Trp Leu Gly Ile Pro Gln	225 230 235	Lys Arg Ile Val Asp Pro Asn Val Asp Glu His Ser	20 245 250	Ile Ala Leu	80 265 265	Asn Gln Arg	
WO 2004/055519 33/335			<210> 9	<211> 2647	5 <212> PRT	<213> Homo sapiens	<220>	<221> Filamin A	<222> (1)(2647)	10 <223> Accession No. P21333	<400> 9		Met Ser Ser His Ser Arg Ala Gly Gln Ser Ala Ala (. 10	15 Pro Gly Gly Gly Val Asp Thr Arg Asp Ala Glu Met Pro A	20 25	Lys Asp Leu Ala Glu Asp Ala Pro Trp Lys Lys Ile Gln (35 40 45	Phe Thr Arg Trp Cys Asn Glu His Leu Lys Cys Val Ser 1	20 50 55 . 60	Ala Asn Leu Gln Thr Asp Leu Ser Asp Gly Leu Arg Leu :	70 75	Leu Glu Val Leu. Ser Gln Lys Lys Met His Arg Lys His i	

014057 WO 2004/055519 PCT/EP2003/014057	Ser Ala Cys Arg Ala Val Gly Arg Gly Leu Gln Pro Lys Gly Val Arg 485 496 Val Lys Glu Thr Ala Asp Phe Lys Val Tyr Thr Lys Gly Ala Gly Ser	500 505 510 510 510 505 510 510 510 510	Asp Leu Gly Asp Gly Val Tyr Gly Phe 535 540 Gly Thr Tyr Ile Val Thr Ile Trr	10 545 550 555 560 Ile Gly Arg Ser Pro Phe Glu Val Lys Val Gly Thr Glu Cys Gly Asn 565 570 575 Gln Lys Val Arg Ala Trp Gly Pro Gly Leu Glu Gly Cly Val Val Gly	580 585 590 15 Lys Ser Ala Asp Phe Val Val Glu Ala Ile Gly Asp Val Gly Thr 595 600 605 Leu Gly Fhe Ser Val Glu Gly Pro Ser Gln Ala Lys Ile Glu Cys Asp	610 615 620 Asp Lys Gly Asp Gly Ser Cys Asp Val Arg Tyr Trp Pro Gln Glu Ala 20 625 630 635 640 Gly Glu Tyr Ala Val His Val Leu Cys Asn Ser Glu Asp Ile Arg Leu 645 650 655	Ser Pro Phe Met Ala Asp Ile Arg Asp Ala Pro Gln Asp Phe His Pro 660 665 670
WO 2004/055519 PCT/EP2003/014057	Pro Gly Ile Glu Fro Thr Gly Asn Met Val Lys Lys Arg Ala Glu Phe 290 Thr Val Glu Thr Arg Ser Ala Gly Gln Gly Glu Val Leu Val Tyr Val	305 310 315 320 Glu Ale Lys Val Thr Ale Asn Asn 320 320	Phe Ser Val Trp Tyr Val Pro Glu Val 345 350 Val Leu Phe Ala Gly Gln His Ile Ala	Pro Phe Glu Val Tyr Val Asp Lys Ser Gln Gly Asp Ala Ser Lys Val 370 375 380 Thr Ala Gln Gly Pro Gly Leu Glu Pro Ser Gly Asn Ile Ala Asn Lys	395 400 Thr Thr Tyr Phe Glu Ile Phe Thr Ala Gly Ala Gly Thr Gly Glu Val 405 410 415 Glu Vel Vel Ile Gln Asp Pro Met Gly Gln Lys Gly Thr Val Glu Pro	420 Gln Leu Glu Ala Arg Gly Asp Ser Thr Tyr Arg Cys Ser Tyr Gln Pro 435 440 445 Thr Met Glu Gly Val His Thr Val His Val Thr Phe Ala Gly Val Pro 450 450 450	Ile Pro Arg Ser Pro Tyr Thr Val Thr Val Gly Gln Ala Cys Asn Pro 465 470 475 480

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Asp Arg Val Lys Ala Arg Gly Pro Gly Leu Glu Lys Thr Gly Val Ala	Lys Val Glu Pro Ser His Asp Ala Ser Lys Val Lys Ala Glu Gly Pro
675 680 685	865 870 875 880
Vel Asn Lys Pro Ala Glu Phe Thr Val Asp Ala Lys His Gly Gly Lys	Gly Leu Ser Arg Thr Gly Val Glu Leu Gly Lys Pro Thr His Phe Thr
690 695 700	895 890 895
5 Aia Pro Leu Arg Val Gln Val Gln Asp Asn Glu Gly Cys Pro Val Glu	5 Val Asn Ala Lys Ala Ala Gly Lys Gly Lys Leu Asp Val Gln Phe Ser
705 710 715 720	900 905 910
Ale Leu Val Lys Asp Asn Gly Asn Gly Thr Tyr Ser Cys Ser Tyr Val	Gly Leu Thr Lys Gly Asp Ala Val Arg Asp Val Asp Ile Ile Asp His
725 730 735	915 920 925
Pro Arg Lys Pro Val Lys His Thr Ala Met Val Ser Trp Gly Gly Val	His Asp Asn Thr Tyr Thr Val Lys Tyr Thr Pro Val Gln Gln Gly Pro
10 740 745 750	10 930 935 940
Ser Ile Pro Asn Ser Pro Phe Arg Val Asn Val Gly Ala Gly Ser His	Val Gly Val Asn Val Thr Tyr Gly Gly Asp Pro Ile Pro Lys Ser Pro
755 760 765	945 950 955
Pro Aen Lys Val Lys Val Tyr Gly Pro Gly Val Ala Lys Thr Gly Leu	Phe Ser Val Ala Val Ser Pro Ser Leu Asp Leu Ser Lys Ile Lys Val
770 775 780	965 970 975
15 Lys Ala His Glu Pro Thr Tyr Phe Thr Val Asp Cys Ala Glu Ala Gly	is Ser Gly Leu Gly Glu Lys Val Asp Val Gly Lys Asp Gln Glu Phe Thr
785 790 795 800	086 586 086
Gln Gly Asp Val Ser Ile Gly Ile Lys Cys Ala Pro Gly Val Val Gly	Val Lys Ser Lys Gly Ala Gly Gly Gln Gly Lys Val Ala Ser Lys Ile
805 . 810 815	1000 1005
Pro Ala Glu Ala Asp Ile Asp Phe Asp Ile Ile Arg Asn Asp Asn Asp	Val Gly Pro Ser Gly Ala Ala Val Pro Cys Lys Val Glu Pro Gly
20 820 825 830	.20 1010 1015 1020
Thr Phe Thr Val Lys Tyr Thr Pro Arg Gly Ala Gly Ser Tyr Thr Ile	Leu Gly Ala Asp Asn Ser Val Val Arg Phe Leu Pro Arg Glu Glu
835 840 845	1025 1030 1035
Met Val Leu Phe Ala Asp Gin Ala Thr Pro Thr Ser Pro Ile Arg Val	Gly Pro Tyr Glu Val Glu Val Thr Tyr Asp Gly Val Pro Val Pro
850 855 860	1040 1045 1050

WO 2004/055519 PCT/EP2003/014057	Lys Tyr Gly Gly Gln Pro Val Pro Asn Phe Pro Ser Lys Leu Gln 1235 1246	Pro Ala Val Asp Thr Ser Gly Val Gln		5 Gly Ile Glu Gly Gln Gly Vel Phe Arg Glu Ala Thr Glu Phe	1265 1270 1275	Ser Val Asp Ala Arg Ala Leu Thr Gln Thr Gly Gly Pro His Val	1280 1285 1290	Lys Ala Arg Val Ala Asn Pro Ser Gly Asn Leu Thr Glu Thr Tyr	10 1295 1300 1305	Val Gln Asp Arg Gly Asp Gly Met Tyr Lys Val Glu Tyr Thr Pro	1310 1315 1320	Tyr Glu Glu Gly Leu His Ser Val Asp Val Thr Tyr Asp Gly Ser	1325 1330 1335	15 Pro Val Pro Ser Ser Pro Phe Gln Val Pro Val Thr Glu Gly Cys	1340 1345 1350	Asp Pro Ser Arg Val Arg Val His Gly Pro Gly Ile Gln Ser Gly	1355 1360 1365	The The Asn Lys Pro Asn Lys Phe The Val Glu The Arg Gly Ala	20 1370 1375 1380	Gly Thr Gly Gly Leu Gly Leu Ala Val Glu Gly Pro Ser Glu Ala	1385 1390 1395	Lys Met Ser Cys Met Asp Asn Lys Asp Gly Ser Cys Ser Val Glu	
PCT/EP2003/014057	GLY Ser Pro Phe Pro Leu Glu Ala Val Ala Pro Thr Lys Pro Ser 1055 1060 1065	Lys Val Lys Ala Phe Gly Pro Gly Leu Gln Gly Gly Ser Ala Gly	1080	Ser Pro Ala Arg Phe Thr Ile Asp Thr Lys Gly Ala Gly Thr Gly	1095	Gly Leu Gly Leu Thr Val Glu Gly Pro Cys Glu Ala Gln Leu Glu	1110	Cys Leu Asp Asn Gly Asp Gly Thr Cys Ser Val Ser Tyr Val Pro	1125	Thr Glu Pro Gly Asp Tyr Asn Ile Asn Ile Leu Phe Ala Asp Thr	1140	·His Ile Pro Gly Ser Pro Phe Lys Ala His Val Val Pro Cys Phe	1155	Ser Lys Val Lys Cys Ser Gly Pro Gly Leu Glu Arg Ala	1170	Gly Glu Val Gly Gln Phe Gln Val Asp Cys Ser Ser Ala	1185	Ala Glu Leu Thr Ile Glu Ile Cys Ser Glu Ala Gly Leu	1200	Glu Val Tyr Ile Gln Asp His Gly Asp Gly Thr His Thr	1215	ile thr Tyr ile Pro Leu Cys Pro Gly Ala Tyr thr Val thr ile	
39/335	Glu Ala V 1060	Pro Gly L	1075	r ile Asp T	1090	al Glu Gly P	1105	ABP Gly Thr C	1120	Tyr Asn Ile A	1135	Pro Phe Lys Al	1150	ys Cys Ser G	1165	lly Gln Phe Gl	1180	r ile Glu'il	1195	le Gln Asp Hi	1210	eu Cys Pro Gl	

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		41/335			42/335
	Tyr Ile. Pro Tyr Glu Al	Tyr Ile Fro Tyr Glu Ala Gly Thr Tyr Ser Leu Asn Va	Val Thr Tyr		-
	1415	1420 1425			
	Gly Gly His Gln Val Pr	Gly Gly His Gln Val Pro Gly Ser Pro Phe Lys Val Pr	o Val His	Thr His Ile Gln Asp Asn His Asp Gly Thr Tyr Thr Val Ala Tyr	p Gly Thr Tyr Thr Val Ala Tyr
	1430	1435 1440		1595 1600	1605
un.	5 Asp Val Thr Asp Ala Se	Asp Val Thr Asp Ala Ser Lys Val Lys Cys Ser Gly Pr	Pro Gly Leu	5 Val Pro Asp Val Thr Gly Arg Tyr Thr Ile Leu Ile Lys Tyr Gly	r Thr ile beu ile bys Tyr Gly
	1445	1450 1455		1610 1615	. 1620
	Ser Pro Gly Met Val Ar	Ser Pro Gly Met Val Arg Ala Asn Leu Pro Gln Ser Ph	ie Gln Val	Gly Asp Glu Ile Pro Phe Ser Pro Tyr Arg Val Arg Ala Val Pro	o Tyr Arg Val Arg Ala Val Pro
	1460	1465 1470	. :	1625 1630	1635
	Asp Thr Ser Lys Ala Gl	Ser Lys Ala Gly Val Ala Pro Leu Gln Val Ly	rs Val Gln	Thr Gly Asp Ala Ser Lys Cys Thr Val Thr Val Ser Ile Gly Gly	r Val Thr Val Ser Ile Gly Gly
9	0 1475	1480 1485	01	1640 1645	1650
	Gly Pro Lys Gly Leu Va	Gly Pro Lys Gly Leu Val Glu Pro Val Asp Val Val Asp Asn Ala	p Asn Ala	His Gly Leu Gly Ala Gly Ile Gly Pro Thr Ile Gln Ile Gly Glu	y Pro Thr Ile Gln Ile Gly Glu
	1490	1495		1655 1660	1665
	Asp Gly Thr Gln Thr Val Asn	Tyr Val Pro Ser Arg	Glu Gly Pro	Glu Thr Val Ile Thr Val Asp Thr Lys Ala Ala Gly Lys Gly Lys	r Lys Ala Ala Gly Lys Gly Lys
	1505	1510 1515		1670 1675	1680
51	Tyr Ser	lle Ser Val Leu Tyr Gly Asp Glu Glu Val Pr	co Arg Ser	15 Val Thr Cys Thr Val Cys Thr Pro Asp Gly Ser Glu Val Asp Val	o Asp Gly Ser Glu Val Asp Val
	1520	1525		1685	1695
	Pro Phe Lys Val Lys Va	Lys Val Lys Val Leu Pro Thr His Asp Ala Se	Ser Lys Val	Asp Val Val Glu Asn Glu Asp Gly Thr Phe Asp Ile Phe Tyr Thr	y Thr Phe Asp Ile Phe Tyr Thr
	, 1535	1540 1545		1700 1705	1710
	Lys Ala Ser Gly Pro Gl	Ser Gly Pro Gly Leu Asn Thr Thr Gly Val Pr	Pro Ala Ser	Ala Pro Gln Pro Gly Lys Tyr Val Ile Cys Val Arg Phe Gly Gly	d ile Cys Val Arg Phe Gly Gly
70	0 1550	1555 1560	22	20 1715 1720	1725
	Leu Pro Val Glu Phe Th	Leu Pro Val Glu Phe Thr lle Asp Ala Lys Asp Ala Gl	Gly Olu Gly	Glu His Val Pro Asn Ser Pro Phe Gln Val Thr Ala Leu Ala Gly	e Gln Val Thr Ala Leu Ala Gly
	. 1565	1570 1575		1730 1735	1740
	Leu Leu Ala Val Gln Il	Leu Leu Ala Val Gin Ile Thr Asp Pro Glu Gly Lys Pr	Pro Lys Lys	Asp Gin Pro Ser Val Gin Pro Pro Leu Arg Ser Gin Gin Leu Ala	o Leu Arg Ser Gln Gln Leu Ala
	1580	1585 . 1590		1745 1750	1755

	WO 2004/055519	5219	43/335	PCT/EP2003/014057			WO 2004/055519	44/335	PCT/EP2003/014057
	Pro Gln	Pro Gln Tyr Thr Tyr Ala Gln	Gly Gly Gln Gln Thr	Trp Ala Pro			Asn Glu Gln His Val Pro Gly	ro Gly Ser Pro Phe Thr Ala Arg Val Thr	g Val Thr
	1760	1765	5 1770				1940	1945 1950	
	Glu Arg		Pro Leu Val Gly Val Asn Gly Leu Asp. Val	Thr Ser Leu			Gly Asp Asp Ser Met A	Gly Asp Asp Ser Wet Arg Met Ser His Leu Lys Val Gly Ser Ala	y Ser Ala
	1775	1780	0 1785				1955	1960 1965	
S.	Arg Pro		Phe Asp Leu Val Ile Pro Phe Thr Ile Lys	Lys Gly Glu	•	IG.	Ala Asp Ile Pro Ile A	Ala Asp Ile Pro Ile Asn Ile Sex Glu Thr Asp Leu Ser Leu Leu	r Leu Leu
	1790	1795	1800				1970	1975	
	ile Thr	Gly Glu Val Arg Met	ile Thr Gly Glu Val Arg Met Pro Ser Gly Lys Val)	Ala Gln Pro			Thr Ala Thr Val Val Pro Pro	o Pro Ser Gly Arg Glu Glu Pro Cys Leu	o Cys Leu
	1805	1810	1815				1985	1990 1995	•
	Thr Ile		Thr Asp Asn Lys Asp Gly Thr Val Thr Val 1	Arg Tyr Ala			Leu Lys Arg Leu Arg A	Leu Lys Arg Leu Arg Asn Gly His Val Gly Ile Ser Phe Val Pro	e Val Pro
01	1820	1825	1830			10	2000	2005 2010	
	Pro Ser	Glu Ala Gly Leu His	Pro Ser Glu Ala Gly Leu Hís Glu Met Asp Ile Arg 1	Tyr Asp Asn			Lys Glu Thr Gly Glu H	Lys Glu Thr Gly Glu His Leu Val His Val Lys Lys Asn Gly Gln	n Gly Gln
	1835	1840	1845	·		•	2015	2020 2025	
	Met His	Ile Pro Gly Ser Pro	Met His lie Pro Gly Ser Pro Leu Gln Phe Tyr Val A	Asp Tyr Val	•		His Val Ala Ser Ser Pa	His Val Ala Ser Ser Pro Ile Pro Val Val Ile Ser Gl	Gln Ser Glu
	1850	1855	1860				2030	2035 2040	
15	Asn Cys	Gly His Val Thr Ala	Asn Cys Gly His Val Thr Ala Tyr Gly Pro Gly Leu T	Thr His Gly		· 15	Ile Gly Asp Ala Ser An	Ile Gly Asp Ala Ser Arg Val Arg Val Ser Gly Gln Gly Leu His	y Leu His
	1865	1870	1875				. 2045	2050 2055	
	Val Val	Asn Lys Pro Ala Thr	Val Val Asn Lys Pro Ala Thr Phe Thr Val Asn Thr L	Lys Asp Ala		٠	Glu Gly His Thr Phe Gl	Glu Gly His Thr Phe Glu Pro Ala Glu Phe Ile Ile Asp Thr Arg	p Thr Arg
	1880	1885	1890				2060	2065 2070	
	Gly Glu	Gly Gly Leu Ser Leu	ly Pro	Ser Lys Ala			Asp Ala Gly Tyr Gly Gl	Asp Ala Gly Tyr Gly Gly Leu Ser Leu Ser Ile Glu Gly Pro Ser	y Pro Ser
20	1895	1900	1905			20	2075	2080 2085	
	Glu Ile	Ser Cys Thr Asp Asn	Glu ile Ser Cys Thr Asp Asn Gln Asp Gly Thr Cys S	Ser Val Ser			Lys Vel Asp Ile Asn Th	Lys Vel Asp Ile Asn Thr Glu Asp Leu Glu Asp Gly Thr Cys Arg	r Cys Arg
	1910	1915	1920				2090	2095 2100	
	Tyr Leu	Pro Val Leu Pro Gly	Tyr Leu , Pro Val Leu Pro Gly Asp Tyr Ser Ile Leu Va	al Lys Tyr			Val Thr Tyr Cys Pro Th	Val Thr Tyr Cys Pro Thr Glu Pro Gly Asn Tyr Ile Ile Asn Ile	e Asn Ile
	1925	1930	1935			•	2105	2110 2115	

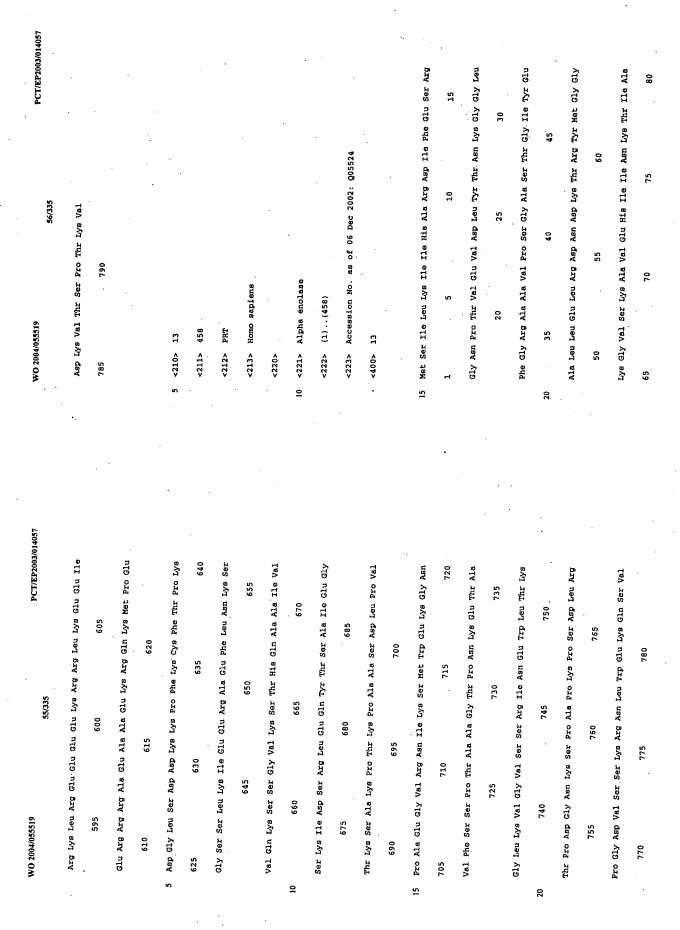
WO 2004/055519 46/335 PCT/EP2003/014057	Val Gln Glu Pro Gly Asp Tyr Glu Val Ser Val Lys Phe Asn Glu	2300 2305 2310	Glu His Ile Pro Asp Ser Pro Phe Val Val Pro Val Ala Ser Pro	2315 2320 2325	5 Ser Gly Asp Ala Arg Arg Leu Thr Val Ser Ser Leu Gln Glu Ser	2330 2335 2340	Gly Leu Lys Val Asn Gln Pro Ala Ser Phe Ala Val Ser Leu Asn	2345 2350 2355	Gly Ala Lys Gly Ala Ile Asp Ala Lys Val His Ser Pro Ser Gly	10 2360 2365 2370	Ala Leu Glu Glu Cys Tyr Val Thr Glu Ile Asp Gln Asp Lys Tyr	2375 2380 2385	Ala Val Arg Phe Ile Pro Arg Glu Asn Gly Val Tyr Leu Ile Asp	2390 2395 2400	15 Val Lys Phe Asn Gly Thr His Ile Pro Gly Ser Pro Phe Lys Ile	2405 2410 2415	Arg Val Gly Glu Pro Gly His Gly Gly Asp Pro Gly Leu Val Ser	2420 2425 2430	Ala Tyr Gly Ala Gly Leu Glu Gly Gly Val Thr Gly Asn Pro Ala	20 2435 2440 2445	. Glu Phe Val Val Asn Thr Ser Asn Ala Gly Ala Gly Ala Leu Ser	2450 2455 2460	Val Thr Ile Asp Gly Pro Ser Lys Val Lys Met Asp Cys Gln Glu	2465 2470 2475		
WO 2004/055519 PCT/EP2003/014057 45/335	Lys Phe Ala Asp Gln His Val Pro Gly Ser Pro Phe Ser Val Lys	2120 2125 2130	Val Thr Gly Glu Gly Arg Val Lys Glu Ser Ile Thr Arg Arg	2135 2140 2145	5 Arg Ala Pro Ser Val Ala Asn Val Gly Ser His Cys Asp Leu Ser	2150 2155 2160	Leu Lys Ile Pro Glu Ile Ser Ile Gln Asp Met Thr Ala Gln Val	2165 2170 2175	Thr Ser Pro Ser Gly Lys Thr His Glu Ala Glu Ile Val Glu Gly	. 10 2180 2185 2190	Glu Asn His Thr Tyr Cys Ile Arg Phe Val Pro Ala Glu Met Gly	2195 2200 · 2205	Thr His Thr Val Ser Val Lys Tyr Lys Gly Gln His Val Pro Gly	2210 2215 2220	. Ser Pro Phe Gln Phe Thr Val Gly Pro Leu Gly Glu Gly Gly Ala	2225 2230 2235	His Lys Val Arg Ala Gly Gly Pro Gly Leu Glu Arg Ala Glu Ala	2240 2245 2250	. Gly Vel Pro Ala Glu Phe Ser Ile Trp Thr Arg Glu Ala Gly Ala	20 2255 2260 2265	Gly Gly Leu Ala Ile Ala Val Glu Gly Pro Ser Lys Ala Glu Ile	2270 2275 2280	Ser Phe Glu Asp Arg Lys Asp Gly Ser Cys Gly Val Ala Tyr Val	2285 2290 2295		

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				48/333
Cys Pro Glu Gly Tyr Arg Va	Glu Gly Tyr Arg Val Thr Tyr Thr Pro Met Al	Ala Pro Gly		
2480 24	2485 2490	4.		
Ser Tyr Leu Ile Ser Ile Lys Tyr Gly Gly Pro Tyr Hi	B TYr Gly Gly Pro Tyr	His Ile Gly	<210> 10	
2495 25	2500 2505		<211> 199	
5 Gly Ser Pro Phe Lys Ala Lys Val Thr Gly Pro Arg Leu Val Ser	s Val Thr Gly Pro Arg	Leu Val Ser	5 <212> PRT	
2510 25:	2515 . 2520		<213> Homo sapiens	
Asn His Ser Leu His Glu Thr Ser Ser Val Phe Val		Asp Ser Leu	<220>	
2525 2530	30 2535		<221> Transgelin 2	
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Lys Ala Tyr Val Gly Gln Lys	Ser Ser Phe Thr Val	Asp Cys Ser	Met Ala Asn Arg Gly Pro Ala	Met Ala Asn Arg Gly Pro Ala Tyr Gly Leu Ser Arg Glu Val Gln Gln
2570 2575	75 2580			10 15
15 Lys Ala Gly Asn Asn Met Leu Leu Val Gly Val His Gl	ı Leu Val Gly Val His	y Pro Arg	15 Lys Ile Glu Lys Gln Tyr Asp	Lys Ile Glu Lys Gln Tyr Asp Ala Asp Leu Glu Gln Ile Leu Ile Gln
2585 2590	30 2595		20	25 30
Thr Pro Cys Glu Glu Ile Leu Val Lys His Val Gly		Ser Arg Leu	Trp Ile Thr Thr Gln Cys Arg	Trp lle Thr Thr Gln Cys Arg Lys Asp Vel Gly Arg Pro Gln Pro Gly
2600 2605	2610		38	40 45
Tyr Ser Val Ser Tyr Leu Leu Lys Asp Lys Gly Glu		Tyr Thr Leu	Arg Glu Asn Phe Gln Asn Trp	Arg Glu Asn Phe Gln Asn Trp Leu Lys Asp Gly Thr Vel Leu Cys Glu
20 2615 . 2620	2625		20 50 55	09
Val Val Lys Trp Gly His Glu His Ile Pro Gly Ser		Pro Tyr Arg	Leu Ile Asn Ala Leu Tyr Pro	Leu ile Asn Ala Leu Tyr Pro Glu Gly Gln Ala Pro Val Lys Lys Ile
2630. 2635	15 2640		. 70	75 80
Val Val Val Pro			Gln Ala Ser Thr Met Ala Phe	Gln Ala Ser Thr Met Ala Phe Lys Gln Met Glu Gln Ile Ser Gln Phe
2645			.	56 06

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	49/335		50/335
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115	120 125		1 5 10 15
5 Leu Met Asn Leu Gly Gly Le	Leu Met Asn Leu Gly Gly Leu Ala Val Ala Arg Asp Asp Gly Leu Phe	y Leu Phe	5 Leu Gln Gln Ala Asp Glu Ala Glu Asp Arg Ala Gln Gly Leu Gln
130 135	5 140		20 25 30
Ser Gly Asp Pro Asn Trp Pho	Ser Gly Asp Pro Asn Trp Phe Pro Lys Lys Ser Lys Glu Asn Pro Arg	n Pro Arg	Arg Glu Leu Asp Gly Glu Arg Glu Arg Arg Glu Lys Ala Glu Gly Asp
145 150	155	160	35 40 45
Asn Phe Ser Asp Asn Gln Le	Asn Phe Ser Asp Asn Gln Leu Gln Glu Gly Lys Asn Val Ile Gly Leu	e Gly Leu	Val Ala Ala Leu Agn Arg Arg Ile Gln Leu Val Glu Glu Glu Leu Asp
10 165	170	175	10 50 55 60
Gln Met Gly Thr Asn Arg Gly Ala Ser Gln Ala Gly Met		thr Gly Tyr	Arg Ala Gin Giu Arg Leu Ala Thr Ala Leu Gin Lys Leu Giu Giu Ala
180	185		65 70 75 80
Gly Met Pro Arg Gln Ile Leu	ם		Glu Lys Ala Ala Asp Glu Ser Glu Arg Gly Met Lys Val Ile Glu Asn
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51/335		52/335	
Lys Tyr Ser Glu Lys Glu Asp Lys Tyr Glu Glu Glu Ile Lys Leu Leu	e Lys Leu Leu	Glu Met Arg Leu Glu Ala Glu Arg Ile Ala Tyr Gln Arg Asn Asp Asp	Asp
180 185	190	20 25 30	
Ser Asp Lys Leu Lys Glu Ala Glu Thr Arg Ala Glu Phe Ala Glu Arg	e Ala Glu Arg	Asp Glu Glu Glu Ala Ala Arg Glu Arg Arg Arg Arg Ala Arg Gln Glu	ı Glu
195 200 205		35 40 45	
5 Thr Val Ala Lys Leu Glu Lys Thr Ile Asp Asp Leu Glu Glu Lys Leu	n Glu Lys Leu	5 Arg Leu Arg Gln Lys Gln Glu Glu Ger Leu Gly Gln Val Thr Asp	. Asp
210 215 220		09 55 05	
Ala Gin Ala Lys Giu Giu Asn Val Gly Leu His Gin Thr Leu Asp Gin	r Leu Asp Gln	Gin Val Glu Val Asn Ala Gln Asn Ser Val Pro Asp Glu Glu Ala Lys	Lys
225 230 235	240	65. 70 75	. 80
Thr Leu Asn Glu Leu Asn Cys Ile		Thr Thr Thr Asn Thr Gln Val Glu Gly Asp Asp Glu Ala Ala Phe	. Phe
10 245	•	10 85 90 95	
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Met Asp Asp Phe Glu Arg Arg Arg Glu Leu Arg Arg Gln Lys Arg	1 Lys Arg Glu	Glu Glu Glu Lys Pro Lys Arg Gly Ser Ile Gly Glu Asn Gln Val	ı val
1 5 10 .	15	205 200 205	

WO 2004/055519 54/335	Glu Thr Lys lie Lys Gly Glu Lys Val Glu Gln Lys lle Glu Gly Lys	405 410 415	Trp Val Asn Glu Lys Ala Gln Glu Asp Lys Leu Gln Thr Ala Val	420 425 430	5 Leu Lys Lys Gln Gly Glu Glu Lys Gly Thr Lys Val Gln Ala Lys Arg	435 440 445	Glu Lys Leu Gln Glu Asp Lys Pro Thr Phe Lys Lys Glu Glu Ile Lys	450 455 460	Asp Glu Lys Ile Lys Lys Asp Lys Glu Pro Lys Glu Glu Val Lys Ser	10 465 470 475 480	Phe Met Asp Arg Lys Lys Gly Phe Thr Glu Val Lys Ser Gln Asn Gly	485 490 495	Glu Phe Met Thr His Lys Leu Lys His Thr Glu Asn Thr Phe Ser Arg	500 505 510	15 Pro Gly Gly Arg Ala Ser Val Asp Thr Lys Glu Ala Glu Gly Ala Pro	515 520 525	. Gln Val Glu Ala Gly Lys Arg Leu Glu Glu Leu Arg Arg Arg Arg Gly	530 535 540	Glu Thr Glu Ser Glu Glu Phe Glu Lys Leu Lys Gln Lys Gln Gln Glu	20 545 550 555 560	Ala Ala Leu Glu Leu Glu Glu Leu Lys Lys Arg Glu Glu Arg Arg	565 570 575	Lys Val Leu Glu Glu Glu Glu Gln Arg Arg Lys Gln Glu Glu Ala Asp	280 585 590
WO 2004/055519 53/335 SCT/EP2003/014057	Glu Val Met Val Glu Glu Lys Thr Thr Glu Ser Gln Glu Glu Thr Val	210 215 220	Val Met Ser Leu Lys Asn Gly Gln Ile Ser Ser Glu Glu Pro Lys Gln .	225 230 235 240	5 Glu Glu Glu Arg Glu Gln Gly Ser Asp Glu Ile Ser His His Glu Lys	245 250 255	Met Glu Glu Glu Asp Lys Glu Arg Ala Glu Ala Glu Arg Ala Arg Leu	260 265 270	Glu Ala Glu Glu Arg Glu Arg Ile Lys Ala Glu Gln Asp Lys Lys Ile	10 275 280 285	Ala Asp Glu Arg Ala Arg Ile Glu Ala Glu Glu Lyg Ala Ala Ala Gln	290 295 300	Glu Arg Glu Arg Arg Glu Ala Glu Glu Arg Glu Arg Met Arg Glu Glu	305 310 315 320	15 Glu Lys Arg Ala Ala Glu Glu Arg Gln Arg Ile Lys Glu Glu Glu Lys	325 330 335	Arg Ala Ala Glu Glu Arg Gln Arg Ile Lys Glu Glu Glu Lys Arg Ala	. 340 345 . 350	Ala Glu Glu Arg Gln Arg Ile Lys Glu Glu Glu Lys Arg Ala Ala Glu	20 355 360 365	Glu Arg Gln Arg Ala Arg Ala Glu Glu Glu Glu Lys Ala Lys Val Glu	370 375 380	Glu Gln Lys Arg Asn Lys Gln Leu Glu Glu Lys Lys Arg Ala Met Gln	385 390 395 400



014057 WO 2004/055519 PCT/EP2003/014057 58/335	Pro Asp Asp Pro Ser Arg Tyr Ile Ser Pro Asp Gln Leu Ala Asp Leu	275 280 285	Tyr Lys Gly Phe Val Leu Gly His Ala Val Lys Asn Tyr Pro Val Gly	290 295 300	5 Val. Ser Ile Glu Asp Pro Pro Phe Asp Gln Asp Asp Trp Gly Ala Trp	305 310 315 320	Lys Lys Leu Phe Thr Gly Ser Leu Val Gly Ile Gln Val Val Gly Asp	325 330 335	Asp Leu Thr Val Thr Lys Pro Glu Ala Arg Ile Ala Lys Ala Val Glu	10 340 345 350	Glu Val Lys Ala Cys Asn Cys Leu Leu Leu Leu Lys Val Asn Gln Ile	355 360 365	Gly Ser Val Thr Glu Ser Leu Gln Ala Cys Lys Leu Ala Gln Ser Agn	370 . 375 380	15 Gly Trp Gly Val Met Pro Val Ser His Arg Leu Ser Gly Glu Thr Glu	385 390 395 400	Asp Thr Phe Met Ala Asp Leu Val Val Gly Leu Cys Thr Gly Gln Ile	405 410 415	Lys Thr Gly Pro Thr Cys Arg Ser Glu Arg Leu Ala Lys Tyr Asn Gln	20 420 425 430	Leu Leu Arg Ile Glu Glu Ala Glu Ala Gly Ser Lys Ala Arg Phe Ala	435 440 445	. Gly Arg Aen Phe Arg Asn Pro Arg Ile Aen	450 455
WO 2004/055519 57/335 57/335	Pro Ala Leu Ile Sex Lys Asn Val Asn Val Glu Gln Asp Lys Ile	85 06 85	Asp Asn Leu Met Leu Asp Met Asp Gly Ser Glu Asn Lys Ser Lys Phe	100 105 110	5 Gly Ala Asn Ala Ile Leu Gly Val Ser Leu Ala Val Cys Ser Asn Ala	115 120 125	ırg His	130 135 140	Leu Ala Gly Asn Asn Pro Glu Val Ile Leu Pro Val Pro Ala Phe Asn	10 145 150 155 160	Val Ile Asn Gly Gly Ser His Ala Gly Asn Lys Leu Ala Met Gln Glu	165 170 175	Phe Met Ile Pro Pro Cys Gly Ala Asp Arg Phe Asn Asp Ala Ile Arg	180 185 190	15 Ile Gly Ala Glu Val Tyr His Asn Leu Lys Asn Val Ile Lys Glu Lys	195 . 200 205	Tyr Gly Lys Asp Ala Thr Asn Val Gly Asp Glu Gly Gly Phe Ala Pro	210 215 220	Asn Ile Leu Glu Asn Lys Glu Ala Leu Glu Leu Leu Lys Thr Ala Ile	20 225 230 235 240	Gly Lys Ala Gly Tyr Ser Asp Lys Val Val Ile Gly Met Asp Val Ala	245 250 255	Ala Ser Glu Phe Tyr Arg Asp Gly Lys Tyr Asp Leu Asp Phe Asn Ser	260 265 270

	WO 2004/055519	PCT/EP2003/014057	WO 2004/055519	PCT/EP2003/014057
			60/335	
			Glu Ala Phe Lys Asp Ser Glu Gly Tyr Ile Tyr Ala Arg Gly Ala Gln	ly Ala Gln
			100 105 11	110
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٠	<211> 408		115 120 125	
'n	5 <212> PRT		5 Lys Val Glu Gly His Arg Phe Pro Arg Thr Ile His Met Thr Phe Val	hr Phe Val
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	<221> Aminoacylase-1		145 150 155	160
	<222> (1)(408)		Arg Pro Glu Phe His Ala Leu Arg Ala Gly Phe Ala Leu Asp Glu Gly	sp Glu Gly
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			180 185 190	00
	Met Thr Ser Lys Gly Pro Glu Glu Glu His Pro Ser Val	er Val Thr Leu Phe	Pro Trp Trp Val Arg Val Thr Ser Thr Gly Arg Pro Gly His Ala Ser	is Ala Ser
	1 55 10	15	195 200 205	
15	Arg Gln Tyr Leu Arg Ile Arg Thr Val Gln Pro Lys Pro	ys Pro Asp Tyr Gly	15 Arg Phe Met Glu Asp Thr Ala Ala Glu Lys Leu His Lys Val Val Asn	ıl Val Asn
	20 25	30	210 215 220	
	Ala Ala Val Ala Phe Phe Glu Glu Thr Ala Arg Gln Leu	iln beu Gly beu Gly	Ser Ile Leu Ala Phe Arg Glu Lys Glu Trp Gln Arg Leu Gln Ser Asn	n Ser Asn
	35 40	45	225 230 235	240
	Cys Gln Lys Val Glu Val Ala Pro Gly Tyr Val Val Thr Val Leu	al Thr Val Leu Thr	Pro His Leu Lys Glu Gly Ser Val Thr Ser Val Asn Leu Thr Lys Leu	r Lys Leu
70	50 55	09	20 245 250	. 552
	Trp Pro Gly Thr Asn Pro Thr Leu Ser Ser Ile Leu Leu Asn Ser His	eu Leu Asn Ser His	Glu Gly Gly Val Ala Tyr Asn Val Ile Pro Ala Thr Met Ser Ala Ser	r Ala Ser
	65 70 75	08	260 . 265 270	
	Thr Asp Val Val Pro Val Phe Lys Glu His Trp Ser His P	er His Asp Pro Phe	Phe Asp Phe Arg Vel Ala Pro Asp Val Asp Phe Lys Ala Phe Glu	e Glu Glu
	96 58	56	275 280 285	

	WO 2004/055519	61/335	-	PCT/EP2003/014057	WO 2004/055519 . 62/335	PCT/EP2003/014057
	Gln Leu Gln Ser Trp Cys Gln Ala Ala Gly Glu Gly Val	Cys Gin Ala Ala Gly		Thr Leu Glu	<222> (1)(277)	
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·	Phe Ala Gln Lys Trp Met His Pro Gln Val Thr Pro Thr Asp Asp Ser	Met His Pro Gln Val	1 Thr Pro Thr Asp	Asp Ser	<400> 15	• .
	305	310	315	320		
ĸ	Asn Pro Trp Trp Ala Ala Phe Ser Arg Val Cys Lys Asp Met Asn Leu	Ala Phe Ser Arg Val	1 Cys Lys Asp Met		5 Met Ser Asp Gln Gln Leu Asp Cys Ala Leu Asp Leu Met Arg Arg Leu	Met Arg Arg Leu
	325	330	•	335	1 10	15
	Thr Leu Glu Pro Glu Ile Met Pro Ala Ala Thr Asp Asn Arg Tyr Ile	ile Met Pro Ala Ala	a Thr Asp Asn Arg	Tyr Ile	Pro Pro Gin Gin Ile Giu Lys Asn Leu Ser Asp Leu Ile Asp Leu Val	ile Asp Leu Val
	340	345	350		. 20 25	30
	Arg Ala Val Gly Val Pro Ala Leu Gly Phe Ser Pro Met Asn Arg Thr	Pro Ala Leu Gly Phe	e Ser Pro Met Asn	Arg Thr	Pro Ser Leu Cys Glu Asp' Leu Leu Ser Ser Val Asp Gln Pro Leu Lys	Gln Pro Leu Lys
01	355	360	365	1	10 35 40	
	Pro Val Leu Leu His Asp His Asp Glu Arg Leu His Glu Ala Val Phe	Asp His Asp Glu Arç	g Leu His Glu Ala	Val Phe	Ile Ala Arg Asp Lys Val Val Gly Lys Asp Tyr Leu Leu Cys Asp Tyr	Leu Cys Asp Tyr
	370	375	380		. 50	
	Leu Arg Gly Val Asp Ile Tyr Thr Arg Leu Leu Pro Ala Leu Ala Ser	ile Tyr Thr Arg Lei	u Leu Pro Ala Leu	Ala Ser	Asn Arg Asp Gly Asp Ser Tyr Arg Ser Pro Trp Ser Asn Lys Tyr Asp	Asn Lys Tyr Asp
	385	390	395	400	65 70 75	. 08
51	15 Val Pro Ala Leu Pro Ser Asp Ser	Ser Asp Ser		-	15 Pro Pro Leu Glu Asp Gly Ala Met Pro Ser Ala Arg Leu Arg Lys Leu	Leu Arg Lys Leu
	405			-	85 90	. 56
					Glu Val Glu Ala Asn Asn Ala Phe Asp Gln Tyr Arg Asp Leu Tyr Phe	Asp Leu Tyr Phe
		-			100 105	110
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	<213> Homo sapiens				130 135 140	
÷	<220>				Lys Gly Cys Trp Asp Ser Ile His Val Val Glu Val Gln Glu Lys Ser	Gln Glu Lys Ser
	<221> F-actin capp	<221> F-actin capping protein beta subunit	bunit		145 150 155	160
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# 1250 1150 1151 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250 1250	WO 2004/044519	
Sec Gly Arg Thr Ale His Tyr Liys Less Thr Val Met Lesu Trp 155 170 170 170 170 170 180 180 180		WO 2004/055519 PCT/EP2003/014057 64/335
175 170 175	Ser Gly Arg Thr Ala His Tyr Lys Leu Thr Ser Thr Val Met Leu Trp	<222> (1) (289)
180 The Ann Lya Ser Gly Ser Gly Thr Reat Ann Lead Gly Gly Ser 190	170	
180 183 190 183 190 184 180 184 180 184 180 184 180 184 180 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184 184	Leu Gln Thr Asn Lys Ser Gly Ser Gly Thr Met Asn Leu Gly Gly Ser	<400> 16
His ite Ala Ann lie Gly Arg Leu Val Glu Ann Ive lie 205 His ite Ala Ann lie Gly Arg Leu Val Glu Ann Hye lie 210 210 213 210 215 Arg Ser Thir Leu Ann Glu Ile Tyr Phe Gly Lye Thr Lye Ann Dla Val 225 Ann Gly Leu Arg Ser Ile Ann Glu Ile Pro Ann Ann Glu Ile Pro Ann Arg Glu Ile Val 226 237 238 230 235 Ann Gly Leu Arg Ser Ile Ann Arg Glu Leu Thr Gln Arg Gln Ile Tyr 260 265 270 270 270 271 271 271 271 272 271 272 272 270 272 272	. 185	
His II has Ann II he dly Arg Leu vol clu Ann II ya II he 210 Arg Ser Thir Leu Ann clu II he pro Ann clu II hya mir clu Ann II ya II he log 211 212 Ann Gly Leu Arg Ser II hap Ala II he pro Ann Glu Ii ya mir clu I han ban ala II han a		
His lie Ala Aan lie Gly Arg Leu Val Glu Aan Tya lie 210 Arg Ser Thr Leu Aan Glu lie Gly Jyg Thr Lyg Aap lie Val 225 Aan Gly Leu Arg Ser lie Aap Ala lie Pro Aap Aan Gln Lyg Phe Lyg Aan Gly Leu Arg Ser lie Aap Ala lie Pro Aap Aan Gln Lyg Phe Lyg 245 250 216 217 218 219 219 210 210 210 211 211 211	200	1 5 10 15
210 215 220 216 217 218 219 219 219 219 219 210 219 210 219 210 219 210 219 210 219 210 219 210 219 210 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219 219	His Ile Ala Asn Ile Gly Arg Leu Val Glu Asp Met Glu Asn Iys Ile	Tyr Arg Val Phe Leu Lys Asn Glu Lys Gly Gln Tyr Ile Ser Pro Phe
Asn Gly Feer Thir Leu Aan Glu Ile Tyr Phe Gly Lys Thir Lys Asp Ile Val 225 Asn Gly Leu Arg Ser Ile Asp Ala Ile Pro Asp Asn Gln Lys Phe Lys 245 245 245 246 256 210 246 257 211 211 212 212 212 212 213 214 226 220 2212 2212 220 2212 2212 220 2212 2212 2212 2212 2212 2212 2212 2212 2212 2212 2212 2212 2212 2212 2212 2212 2212 2212 2212 2212	215	20 . 25 30
131 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140 140	Arg Ser Thr Leu Asn Glu Ile Tyr Phe Gly Lys Thr Lys Asp Ile Val	His Asp Ile Pro Ile Tyr Ala Asp Lys Asp Val Phe His Met Val Val
Asn Gly Leu Arg Ser Ile hap Ala Ile Pro Asp Asn Gln Lys Phe Lyss 245 250 255 Gln Leu Gln Arg Glu Leu Ser Gln Val Leu Thr Gln Arg Gln Ile Tyr 260 265 270 Ile Gln Pro Asp Asn 275 4210- 4211- 289 4212- 4212- 4212- 4215- 4215- 4215- 4215- 4215- 4215- 4220- 789 4221- 789 4221- 789 4221- 789 789 789 789 789 789 789 78	225 230 235	
Sin Feb Gln Arg Glu Leu Ser Gln Val Leu Thr Gln Arg Gln Ile Tyr	Asn Gly Leu Arg Ser ile Asp Ala ile Pro Asp Asn Gln Lys Phe Lys	Glu Val Pro Arg Trp Ser Asn Ala Lys Met Glu ile Ala Thr Lys Asp
Gin Leu Gin Arg Giu Ieu Ser Gin Val Leu Thr Gin Arg Gin Ile Tyr 266 265 270 Ile Gin Pro Asp Asn 275 4215 4215 4215 4215 4215 4215 4215 4220 42215 Inorganic Pyrophosphatase	250	. 09 55 05
156	Gin Leu Gin Arg Glu Leu Ser Gin Val Leu Thr Gin Arg Gin ile Tyr	Pro Leu Asn Pro Ile Lys Gln Asp Val Lys Lys Gly Lys Leu Arg Tyr
116 Gln Pro Asp Asn 15 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 275 2	265	. 07
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<pre><210> 16 <211> 289 <212> PRT <213> Homo sapiens <220> <221> Inorganic Pyrophosphatase</pre>		105
<pre><211> 289 <212> PRT <213> Homo sapiens <220> <221></pre>		Cys Cys Gly Asp Asn Asp Pro Ile Asp Val Cys Glu Ile Gly Ser Lys
Homo sapiens Homo sapiens Thorganic pyrophosphatase	<211>	115 , 120
Homo sapiens Inorganic pyrophosphatase	<212> PRT	Val Cys Ala Arg Gly Glu ile ile Gly Val Lys Val Leu Gly Ile Leu
Inorganic pyrophosphatase	<213> Homo sapiens	135
Inorganic pyrophosphatase	<220>	Ala Met Ile Asp Glu Gly Glu Thr Asp Trp Lys Val Ile Ala Ile Asn
		145 150 155 160

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	Arg Leu Lys Pro Gly Tyr Leu Glu Ala Thr Val Asp T	Thr Val Asp Trp Phe Arg Arg	<222> (1)(250)	
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S	Tyr Lys Val Pro Asp Gly Lys Pro Glu Asn Glu Phe Ala Phe Asn Ala		5 <400> 17	
	195 200	205		
	Glu Phe Lys Asp Lys Asp Phe Ala lle Asp lle lys Ser Thr His	ABP 11e 11e Lys Ser Thr His	Met Ala Asp Asn Phe Ser Leu His Asp Ala Leu Ser Gly Ser Gly Asn	
	210 215	220	1 5 10 15	
	Amp His Trp Lys Ala Leu Val Thr Lys Lys Thr Asn Gly Lys Gly Ile	Lys Thr Asn Gly Lys Gly Ile	Pro Asn Pro Gln Gly Trp Pro Gly Ala Trp Gly Asn Gln Pro Ala Gly	
2	225 230	235 240 10	19 20 25 30	
	Ser Cys Met Asn Thr Teu Ser Glu Ser Pro Phe Lys Cys Asp Pro	Ser Pro Phe Lys Cys Asp Pro	Ala Gly Gly Tyr Pro Gly Ala Ser Tyr Pro Gly Ala Tyr Pro Gly Gln	
	245	250 255	35 40 45	
	Asp Ala Ala Arg Ala Ile Val Asp Ala Leu Pro Pro Pro Cys Glu Ser	Leu Pro Pro Cys Glu Ser	Ala Pro Pro Gly Ala Tyr Pro Gly Gln Ala Pro Pro Gly Ala Tyr His	
	260 265	270	90	
15	Ala Cys Thr Val Pro Thr Asp Val Asp Lys Trp Phe His His Gln Lys		15 Gly Ala Pro Gly Ala Tyr Pro Gly Ala Pro Ala Pro Gly Val Tyr Pro	
	. 275 280	285	65 70 75 80	
	. Asn		Gly Pro Pro Ser Gly Pro Gly Ala Tyr Pro Ser Ser Gly Gln Pro Ser	
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	<212> PRT		Arg Met Leu Ile Thr Ile Leu Gly Thr Val Lys Pro Asn Ala Asn Arg	
	<213> Homo sapiens		130 135 140	

110 All lea by the other and oth	And the cla are city and any state the state than 142 feet and 142 fee		
110 Ala Lou App Phe Glin Arg Gly Ann Amp Vol Ala Phe His Phe Aan 150 155 150 155 150 155 150 155 150 155 150 155 150 155 150 155 150 155 150 155 150 155 150 155 150 155 150 155 150 155 150 150 155 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 1	110 Ala Leu Aup Pie Glin Arg Gliy Ann Amp Vell Ala Pie His Pie Aan 150 150 155 150 155 150	67/33\$	58:335
150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 170 175 175 150 150 150 175 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150	145 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150 150	Ile Ala Leu Asp Phe Gln Arg Gly Asn Asp Vel Ale Phe His Phe Asn	<400> 18
Fig. Arg Phe Asm Clu Asm Asm Arg Val Ile val Cys Asm Thr Lygs Leu Asp Asm Asm Trp Gly Arg Glu Glu Pro Asp His Liss 200 200 205 205 200 205 200 205 205 200 205 200 205 200 205 200 200	Fig. New Pick Asia Ciu Asia Asia Asia Asia Asia Ciu Asia Asia Asia Asia Asia Asia Asia Asia	150 1.55	
153 170 175 175 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185 185	165 170 173 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175 175	Pro Arg Phe Asn Glu Asn Asn Arg Arg Val Ile Val Cys Asn Thr Lys	Met Ser Trp Cys Asn Glu Leu Arg Leu Pro Ala Leu Lys Gln His Ser
180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 181 180 180 181 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180 180	180 And Ann Karp Gly Arg Glu Glu Arg Gln Ser Val Phe Pro Phe 180 181	170	1 5 10 15
180	180	Leu Asp Asn Asn Trp Gly Arg Glu Glu Arg Gln Ser Val Phe Fro Phe	5 Ile Gly Arg Gly Leu Glu Ser His Ile Thr Wet Cys Ile Pro Pro Ser
r Gly Lys Pro Phe Lys Ile Gln Val Leu Val Glu Pro Asp His 195 200 205 195 197 215 220 220 235 240 177 245 245 245 245 245 245 245 2	195 197 198 199 199 200 205 200 205 200 215 220 200 215 220 200 215 220 240 235 240 240 245 245 245 245 246 247 247 248 247 248 249 240 240 240 240 240 240 240 240 240 240	185	. 25
195 200 205 18 Val Ala Val Asn Asp Ala His Leu Leu Gln Tyr Asn His Arg 215 220 216 220 217 220 218 240 219 240 217 245 218 250 219 240 219 245 245 250 19 Phr Homo sapiens 210 202: P45860	195 200 205 19	Glu Ser Gly Lys Pro Phe Lys Ile Gln Val Leu Val Glu Pro Asp His	Tyr Ala Asp Leu Gly Lys Ala Ala Arg Asp 11e Phe Asn Lys Gly Phe
10 215 220 10 10 215 220 10 10 10 10 10 10 10 10 10 10 10 10 10	10 215 220 10 10 10 10 10 10 10 10 10 10 10 10 10	. 200	40
15	10	Phe Lys Val Ala Val Asn Asp Ala His Leu Leu Gln Tyr Asn His Arg	Gly Phe Gly Leu Val Lys Leu Asp Val Lys Thr Lys Ser Cys Ser Gly
### Lys Leu Asn Glu Ile Ser Lys Leu Gly Ile Ser Gly Asp Ile 230	15 Lys Leu Asn Glu Ile Ser Lys Leu Gly Ile Ser Gly Asp Ile 230 235 240 u Thr Ser Ala Ser Tyr Thr Met Ile 245 250 18 347 PRT Homo sapiens (1)(347) Accession No.as of 06 Dec 2002: P45880	215	50 55
230 235 240 u Thr Ser Ala Ser Tyr Thr Met Ile 245 250 18 347 PRT Homo sapiens 20 (1)(347) Accession No.as of 06 Dec 2002: P45880	230 235 240 u Thr Ser Ala Ser Tyr Thr Met Ile 245 250 18 347 Homo sapiens Voltage-dependent anion-selective channel protein 2 (VDAC-2) (1)(347) Accession No.as of 06 Dec 2002: P45880	Val Lys Lys Leu Asn Glu Ile Ser Lys Leu Gly Ile Ser Gly Asp Ile	Val Glu Phe Ser Thr Ser Gly Ser Ser Asn Thr Asp Thr Gly Lys Val
u Thr Ser Ala Ser Tyr Thr Met Ile 245 250 15 1B 347 16 16 PRT Homo sapiens 20 Voltage-dependent anion-selective channel protein 2 (VDAC-2) 20 (1) (347) Accession No.as of 06 Dec 2002: P45880	u Thr Ser Ala Ser Tyr Thr Met Ile 245 250 18 347 PRT Homo sapiens Voltage-dependent anion-selective channel protein 2 (VDAC-2) (1)(347) Accession No.as of 06 Dec 2002: P45880	230 235	70 75
18 18 347 PRT Homo sapiens Voltage-dependent anion-selective channel protein 2 (VDAC-2) (1) (347) Accession No.as of 06 Dec 2002: P45880	18 18 347 PRT Homo sapiens Voltage-dependent anion-selective channel protein 2 (VDAC-2) (1)(347) Accession No.as of 06 Dec 2002: P45880	Asp Leu Thr Ser Ala Ser Tyr Thr Met Ile	Thr Oly Thr Leu Glu Thr Lys Tyr Lys Trp Cys Glu Tyr Gly Leu Thr
18 347 PRT Homo sapiens 20 Voltage-dependent anion-selective channel protein 2 (VDAC-2) (1)(347) Accession No.as of 06 Dec 2002: P45880	18 347 PRT Homo sapiens 19 (1)(347) Accession No.as of 06 Dec 2002: P45880		06
18 347 PRT Homo sapiens Yoltage-dependent anion-selective channel protein 2 (VDAC-2) (1)(347) Accession No.as of 06 Dec 2002: P45880	18 347 PRT Homo sapiens Voltage-dependent anion-selective channel protein 2 (VDAC-2) (1)(347) Accession No.as of 06 Dec 2002; P45880		
18 347 PRT Homo sapiens Coltage-dependent anion-selective channel protein 2 (VDAC-2) (1)(347) Accession No.as of 06 Dec 2002: P45880	18 347 PRT Homo sapiens Yoltage-dependent anion-selective channel protein 2 (VDAC-2) (1)(347) Accession No.as of 06 Dec 2002: P45880		105
PRT Homo sapiens Voltage-dependent anion-selective channel protein 2 (VDAC-2) (1) (347) Accession No.as of 06 Dec 2002; P45880	PRT Homo sapiens Voltage-dependent anion-selective channel protein 2 (VDAC-2) (1)(347) Accession No.as of 06 Dec 2002: P45880		Ile Glu Asp Gln Ile Cys Gln Gly Leu Lys Leu Thr Phe Asp Thr Thr
Homo sapiens Homo sapiens Voltage-dependent anion-selective channel protein 2 (VDAC-2) (1) (347) Accession No.as of 06 Dec 2002; P45880	Homo sapiens Yoltage-dependent anion-selective channel protein 2 (VDAC-2) (1)(347) Accession No.as of 06 Dec 2002: P45880		120
Homo sapiens Voltage-dependent anion-selective channel protein 2 (VDAC-2) (1) (347) Accession No.as of 06 Dec 2002: P45880	Homo sapiens Voltage-dependent anion-selective channel protein 2 (VDAC-2) (1)(347) Accession No.as of 06 Dec 2002: P45880		Phe Ser Pro Ann Thr Gly Lys Lys Ser Gly Lys Ile Lys Ser Ser Tyr
Voltage-dependent anion-selective channel protein 2 (VDAC-2) (1)(347) Accession No.as of 06 Dec 2002: P45880	Voltage-dependent anion-selective channel protein 2 (VDAC-2) (1)(347) Accession No.as of 06 Dec 2002: P45880		130 135
Voltage-dependent anion-selective channel protein 2 (VDAC-2) (1)(347) Accession No.as of 06 Dec 2002: P45880 170 155 155 176 177 177 177 177 177 177 177 177 177	Voltage-dependent anion-selective channel protein 2 (VDAC-2) (1)(347) Accession No.as of 06 Dec 2002: P45880 155 157 178 178 178 178 178 178		Lys Arg Glu Cys Ile Asn Leu Gly Cys Asp Val Asp Phe Asp Phe Ala
(1)(347) Accession No.as of 06 Dec 2002: P45880	(1)(347) Accession No.as of 06 Dec 2002: P45880		150 155
Accession No.as of 06 Dec 2002: P45880	Accession No.as of 06 Dec 2002: P45880		Gly Pro Ala Ile His Gly Ser Ala Val Phe Gly Tyr Glu Gly Trp Leu
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5	, Da		Thr		/a1		Thr	240	뉡		٠,											
PCT/EP2003/014057	Ala Gly Tyr Gln Met Thr Phe Asp Ser Ala Lys Ser Lys Leu Thr Arg	185 190	Asn Asn Phe Ala Val Gly Tyr Arg Thr Gly Asp Phe Gln Leu His Thr	205	Asn Val Asn Asp Gly Thr Glu Phe Gly Gly Ser Ile Tyr Gln Lys Val	220	Cys Glu Asp Leu Asp Thr Ser Val Asn Leu Ala Trp Thr Ser Gly Thr	235	Asn Cys Thr Arg Phe Gly Ile Ala Ala Lys Tyr Gln Leu Asp Pro Thr	250 255	Ala Ser ile Ser Ala Lys Val Asn Asn Ser Ser Leu Ile Gly Val Gly	265 270	Tyr Thr Gln Thr Leu Arg Pro Gly Val Lys Leu Thr Leu Ser Als Leu	. 582	Val Asp Gly Lys Ser Ile Asn Ala Gly Gly His Lys Val Gly Ser Pro	300	Trp Ser Trp Arg Leu Asn Pro Ala Glu Arg Asn Leu Trp Glu Trp Ile	315 320	Ser Glu Asp Leu Ala Leu Ile Tyr Phe His Cys Asp Gln Gln Gln Ala	330 335	Phe Phe Pro Pro Glu Asp Asp Gln Asn Lys Gly	345

WO 2004/055519 PCT/EP2003/014057	Ser Glu Phe Lys Arg Lys Tyr Gly Lys Ser Leu Tyr Tyr 13e Gln	305 310 315 320	Gln Asp Thr Lyg Gly Asp Tyr Gln Lyg Ala Leu Leu Tyr Leu Cys Gly	325 330 335	5 Gly Asp Asp				<210> 20	10 <211> 418	<212> PRT	<213> Homo sapiens	<220>	<221> Collagen-binding protein 2 precursor	15 <222> (1)(418)	<223> Accession No. as of 06 Dec 2002: P50454	<400> 20		Met Arg Ser Leu Leu Leu Ser Ala Phe Cys Leu Leu Glu Ala Ala	20 1 5 10 15	Leu Ala Ala Glu Val Lys Lys Pro Ala Ala Ala Ala Ala Pro Gly Thr	20 25 30	Ala Glu Lys Leu Ser Pro Lys Ala Ala Thr Leu Ala Glu Arg Ser Ala	35 40 45
WO 2004/055519 PCT/EP2003/014057	Glu Leu Lys Ala Ser Met Lys Gly Leu Gly Thr Asp Glu Asp Ser Leu	115 120 125	ile Glu ile ile Cys Ser Arg Thr Asn Gln Glu Leu Gln Glu ile Asn	130 135 140	5 Arg Val Tyr Lys Glu Met Tyr Lys Thr Asp Leu Glu Lys Asp Ile Ile	145 150 155 160	Ser Asp Thr Ser Gly Asp Phe Arg Lys Leu Met Val Ala Leu Ala Lys	165 170 175	Gly Arg Arg Ala Glu Asp Gly Ser Val Ile Asp Tyr Glu Leu Ile Asp	10 180 185 190	Gln Asp Ala Arg Asp Leu Tyr Asp Ala Gly Val Lys Arg Lys Gly Thr	195 200 205	Asp Val Pro Lys Trp Ile Ser Ile Met Thr Glu Arg Ser Val Pro His	210 215 220	15 Leu Gln Lys Val Phe Asp Arg Tyr Lys Ser Tyr Ser Pro Tyr Asp Met	225 230 . 235 240	Leu Glu Ser Ile Arg Lys Glu Val Lys Gly Asp Leu Glu Asn Ala Phe	245 . 250 . 255	Leu Asn Leu Val Gin Cys Ile Gin Asn Lys Pro Leu Tyr Phe Ala Asp	20 260 265 270	Arg Leu Tyr Asp Ser Met Lys Gly Lys Gly Thr Arg Asp Lys Val Leu	275 280 285	Ile Arg ile Met Val Ser Arg Ser Glu Val Asp Met Leu Lys Ile Arg	300 395 300

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70 UU	600
. 09 66 06	250 255
Glu Asn Ile Leu Val Ser Pro Val Val Val Ala Ser Ser Leu Gly Leu	Glu Met Pro Leu Ala His Lys Leu Ser Ser Leu Ile Ile Leu Met Pro
65 70 75 80	260 265 270
5 Val Ser Leu Gly Gly Lys Ala Thr Thr Ala Ser Gln Ala Lys Ala Val	5 His His Val Glu Pro Leu Glu Arg Leu Glu Lys Leu Leu Thr Lys Glu
. 56 06 58	. 275 280 285
heu Ser Ala Glu Gln Leu Arg Asp Glu Glu Val His Ala Gly Leu Gly	Gln Leu Lys Ile Trp Met Gly Lys Met Gln Lys Lys Ala Val Ala Ile
100 . 105 110	290 295 300
Glu Leu Leu Arg Ser Leu Ser Asn Ser Thr Ala Arg Asn Val Thr Trp	Ser Leu Pro Lys Gly Val Val Glu Val Thr His Asp Leu Gin Lys His
10 115 120 125	10 305 . 310 315 320
Lys Leu Gly Ser Arg Leu Tyr Gly Pro Ser Ser Val Ser Phe Ala Asp.	Leu Ala Gly Leu Gly Leu Thr Glu Ala Ile Asp Lys Asn Lys Ala Asp
130 135 140	325 330 335
Asp Phe Val Arg Ser Ser Lys Gln His Tyr Asn Cys Glu His Ser Lys	Leu Ser Arg Met Ser Gly Lys Lys Asp Leu Tyr Leu Ala Ser Val Phe
145 150 155 160	340 345 350
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Ala Ala Gin Thr Thr Asp Gly Lys Leu Pro Giu Val Thr Lys Asp Val	Asp Ile Tyr Gly Arg Glu Glu Leu Arg Ser Pro Lys Leu Phe Tyr Ala
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Glu Arg Thr Asp Gly Ala Leu Leu Val Asn Ala Met Phe Phe Lys Pro	Asp His Pro Phe Ile Phe Leu Val, Arg Asp Thr Gln Ser Gly Ser Leu
20 195 200 205	20 385 390 395 400
His Trp Asp Glu Lys Phe His His Lys Met Val Asp Asn Arg Gly Phe	Leu Phe 11e Gly Arg Leu Val Arg Pro Lys Gly Asp Lys Met Arg Asp
210 215 220	405 410 415
Met Val Thr Arg Ser Tyr Thr Val Gly Val Met Met His Arg Thr	Glu Leu
225 230 235 240	

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	<222> (1)(166)	(166)				jeu Glu Gly Lys Pro Leu	Pro Leu		
2	<223> Access	<223> Accession No. as of 08 ec 2002: P23528	ec 2002: P23528		10		165		
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		85	06	95			.10	. 15	

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01	88	56 . 06		10 1	5 10	. 15
	Ile Leu Ser Met Ala Asn Ala Gly Pro Asn Thr Asn Gly	lly Pro Asn Thr Asn Gly Ser Gln Phe	Phe	Arc	Arg Leu Ala Gin Ile Arg Glu Giu Lys Lys Arg Lys Glu Giu Giu Arg	Arg Lys Glu Glu Glu Arg
	100	105			20 25	30
	Phe Ile Cys Thr Ala Lys Thr (Phe Ile Cys Thr Ala Lys Thr Glu Trp Leu Asp Gly Lys His Val Val	Val	ĹŊĖ	Lys Lys Lys Glu Thr Asp Gln Lys Lys Glu Ala Val Ala Pro Val Gln	Ala Val Ala Pro Val Gln
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	130 135	140			50 55	09
	Phe Gly Ser Arg Asn Gly Lys Thr Ser Lys Lys Ile Thr	hr Ser Lys Lys Ile Thr Ile Ala Asp	Авр	.G1r	Gin Ser Met Gly Leu Thr Pro Glu Ser Pro Ile Val Phe Ser Glu Tyr	Ile Val Phe Ser Glu Tyr
	145 150	155	160	. 59	70	. 80
	Cys Gly Gln Leu Glu			Tr	Trp Val Pro Pro Pro Met Ser Pro Ser Ser Lys Ser Val Ser Thr Pro	Lys Ser Val Ser Thr Pro
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	79/335			80/335	
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130 135	140	01	325	330	335
Gln Val Asp Phe Pro Pro Arg Glu Ile Val Thr	Glu Ile Val Thr Ty	Tyr Thr Lys Glu Thr	Ser Ala Thr Phe Ala Lys Phe	Ser Ala Thr Phe Ala Lys Phe His Pro Asn Leu Val Val Gly Gly Thr	Gly Thr
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Gln Thr Pro Val Met Ala Gln Pro Lys Glu Asp Glu Glu Glu Asp Asp	Pro Lys Glu Asp Glu	u Glu Glu Asp Asp	5 Tyr Ser Gly Gln Ile Val Leu	Tyr Ser Gly Gin ile Val Leu Trp Asp Asn Arg Ser Asn Lys Arg Thr	Arg Thr
165	170	175	355	360 365	
Asp Val Val Ala Pro Lys Pro Pro Ile Glu Pro Glu Glu Glu Lys Thr	Pro Ile Glu Pro Glu	u Glu Glu Lys Thr	Pro Val Gln Arg Thr Pro Leu	Pro Val Gln Arg Thr Pro Leu Ser Ala Ala Ala His Thr His Pro Val	Pro Val
180	185	190	370 375	380	
Leu Lys Lys Asp Glu Glu Asn Asp Ser Lys Ala Pro Pro His Glu Leu	Asp Ser Lys Ala Pro	o Pro His Glu Leu	Tyr Cys Val Asn Val Val Gly	Tyr Cys Val Asn Val Val Gly Thr Gln Asn Ala His Asn Leu Ile Ser	Ile Ser
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Thr Glu Glu Lys Gln Gln Ile Leu His Ser Glu Glu Phe Leu Ser	Ile Leu His Ser Glu	u Glu Phe Leu Ser	Ile Ser Thr Asp Gly Lys Ile	ile Ser Thr Asp Gly Lys Ile Cys Ser Trp Ser Leu Asp Met Leu Ser	Leu Ser
210 . 215	220		405	410	415
Phe Phe Asp His Ser Thr Arg Ile Val Glu Arg Al	Ile Val Glu Arg Ala	a Leu Ser Glu Gln	His Pro Gln Asp Ser Met Glu	His Pro Gin Asp Ser Met Giu Leu Val His Lys Gin Ser Lys Ala Val	Ala Val
225 230	235	240	420	425 430	
Ile Asn Ile Phe Phe Asp Tyr Ser Gly Arg Asp Le	Ser Gly Arg Asp Leu	n Glu Asp Lys Glu	15 Ala Val Thr Ser Met Ser Phe	Ala Val Thr Ser Met Ser Phe Pro Val Gly Asp Val Asn Asn Phe Val	Phe Val
245	250	. 255	435	440 . 445	
Gly Glu Ile Gln Ala Gly Ala Lys Leu Ser Leu Asn Arg Gln Phe Phe	Lys Leu Ser Leu Asn	n Arg Gln Phe Phe	Val Gly Ser Glu Glu Gly Ser	Val Gly Ser Glu Glu Gly Ser Val Tyr Thr Ala Cys Arg His Gly Ser	3ly Ser
. 260	265	270	450 455	460	
Asp Glu Arg Trp Ser Lys His Arg Val Val	Arg Val Val Ser Cys	Ser Cys Leu Asp Trp Ser	Lys Ala Gly Ile Ser Glu Met	Lys Ala Gly Ile Ser Glu Met Phe Glu Gly His Gln Gly Pro Ile Thr	lle Thr
. 275	280	285	20 465 470	475	480
Ser Gln Tyr Pro Glu Leu Leu Vel Ala Ser Tyr Asn Asn Asn Glu Asp	Val Ala Ser Tyr Asn	ı Asn Asn Glu Asp	Gly Ile His Cys His Ala Ala	Gly Ile His Cys His Ala Ala Val Gly Ala Val Asp Phe Ser His Leu	418 Leu
290 . 295	300		485	490	495
Ala Pro His Glu Pro Asp Gly Val Ala Leu Val Trp Asn Met Lys Tyr	Val Ala Leu Val Trp	Asn Met Lys Tyr	Phe Val Thr Ser Ser Phe Asp	Phe Val Thr Ser Ser Phe Asp Trp Thr Val Lys Leu Trp Thr Thr Lys	thr Lys
305 310	. 315	320	.500	505 510	

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Asn Asn Lys Pro Leu Tyr Ser Phe Glu Asp Asn Ala Asp Tyr Val Tyr	<222> (1)(328)
515 520 525	<223> Accession No. as of 09 Dec 2002; Q13011
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Pro Thr Ala Ser Ile Ser Val Glu Gly Asn Pro Ala Leu Asn Arg Val	Arg Arg Leu Thr Gly Ser Asn Tyr Pro Gly Leu Ser Ile Ser Leu Arg
565 570 . 575	20 25 30
Arg Trp Thr His Ser Gly Arg Glu lle Ala Val Gly Asp Ser Glu Gly	Leu Thr Gly Ser Ser Ala Gln Glu Glu Ala Ser Gly Val Ala Leu Gly
10 580 585 590	10 35 40 45
Gin ile Val ile Tyr Asp Val Gly Glu Gin ile Ala Val Pro Arg Asn	Glu Ala Pro Asp His Ser Tyr Glu Ser Leu Arg Val Thr Ser Ala Gln
595 600 595	
Asp Glu Trp Ala Arg Phe Gly Arg Thr Leu Ala Glu Ile Asn Ala Asn	Lys His Val Leu His Val Gin Leu Asn Arg Pro Asn Lys Arg Asn Ala
610 615 620	65 70 75 80
is Arg Ala Asp Ala Glu Glu Ala Ala Thr Arg Ile Pro Ala	is Met Asn Lys Val Phe Trp Arg Glu Met Val Glu Cys Phe Asn Lys Ile
625 . 630 635	56 06 58
	Ser Arg Asp Ala Asp Cys Arg Ala Val Val Ile Ser Gly Ala Gly Lys
	100 105 110
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<212> PRT	Gln Pro Lys Gly Asp Asp Val Ala Arg Ile Ser Trp Tyr Leu Arg Asp
<213> Homo sapiens	130 135 140
<220>	ile ile Thr Arg Tyr Gln Glu Thr Phe Asn Val ile Glu Arg Cys Pro
<221> Deltal,5-delta2,4-dienoyl-CoA isomerase, mitochondrial precursor	145 150 155 160

	WO 2004/055519	PCT/EP2003/014057	WO 2004/055519 PCT/EP2003/014057	4057
	83/335	335	84/335	
	Lys Pro Val 11e Ala Ala Val His Gly Gly Cys 11e Gly Gly Gly Val	ly Gly Cys Ile Gly Gly Gly Val	<210> 25	
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	180	185 . 190	<213> Homo sapiens	
'n	Phe Gln Val Lys Glu Val Asp Val Gly Leu Ala Ala Asp Val Gly Thr	ly Leu Ala Ala Asp Val Gly Thr	<22.0>	
	195 200	205	<221> Ras GTPase-activating-like protein IQGAP1	•
	Leu Glu Arg Leu Pro Lys Val Ile Gly Asn Gln Ser Leu Val Asn Glu	ly Ann Gln Ser Leu Val Asn Glu	<222> (1)(1657)	
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	Leu Ala Phe Thr Ala His Lys Met Met Ala Asp Glu Al	st Ala Asp Glu Ala Leu Asp Ser	<400> 25	
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	Gly Leu Val Ser Arg Val Phe Pro Asp Lys Glu Val Met	ip Lys Glu Val Met Leu Asp Ala	Met Ser Ala Ala Asp Glu Val Asp Gly Leu Gly val Ala Arg Pro His	
	245		1 5 10 15	
	Ala Leu Pro Leu Ala Pro Glu Ile Ser Ser Lys Thr Thr Val Leu Val	r Ser Lys Thr Val Leu Val	Tyr Gly Ser Val Leu Asp Asn Glu Arg Leu Thr Ala Glu Glu Met Asp	
	260 265	5 270 .	20 25 30	
15	Gln Ser Thr Lys Val Asn Leu Leu Tyr Ser Arg Asp His	r Ser Arg Asp His Ser Val Ala	Glu Arg Arg Gln Asn Val Ala Tyr Glu Tyr Leu Cys His Leu Glu	
•	275 280		35 40 45	
	Glu Ser Leu Asn Tyr Val Ala Ser Trp Asn Met Ser Met	p Asn Met Ser Met Leu Gln Thr	Glu Ala Lys Arg Trp Met Glu Ala Cys Leu Gly Glu Asp Leu Pro Pro	
	290 295			
	Gln Asp Leu Val Lys Ser Val Gln Pro Thr Thr Glu Asn	o Thr Thr Glu Asn Lys Glu Leu	Thr Thr Glu Leu Glu Glu Gly Leu Arg Asn Gly Val Tyr Leu Ala Lys	
22 '	305 310	315 320 20	65 70 75 80	
	Lys Thr Val Thr Phe Ser Lys Leu		Leu Gly Asn Phe Phe Ser Pro Lys Val Val Ser Leu Lys Lys Ile Tyr	
	. 325		85 90 95	

Asp Arg Glu Gln Thr Arg Tyr Lys Ala Thr Gly Leu His Phe Arg His

WO 2004/055519 86/335 86/335 Thr Phe Ser Ala Leu Ala Asn Ile Asp Leu ala Jen Glu Glu Glu Glu Glu Glu Glu Ala Asn Ile Asp Leu ala Jen Glu Glu Glu Glu Glu Glu Glu Ala Asp Ileu ala Asp Leu ala Asp Ileu a	305 310 315 315 320	Ala Leu Ala Leu Phe Arg Ala Leu Gln Ser Pro Ala Leu Gly Leu Arg	325 330 335	5 Gly Leu Gin Gin Asn Ser Asp Trp Tyr Leu Lys Gin Leu Leu Ser	340 345 350	Asp Lys Gln Gln Lys Arg Gln Ser Gly Gln Thr Asp Pro Leu Gln Lys	355 360 365	Glu Glu Leu Gln Ser Gly Val Asp Ala Ala Asn Ser Ala Ala Gln Gln	10 370 375 380	Tyr Gln Arg Arg Leu Ala Ala Val Ala Leu Ile Asn Ala Ala Ile Gln	385 390 395 400	Lys Gly Val Ala Glu Lys Thr Val Leu Glu Leu Met Asn Pro Glu Ala	405 410 415	15 Gln Leu Pro Gln Val Tyr Pro Phe Ala Ala Asp Leu Tyr Gln Lys Glu	420 425 430	Leu Ala Thr Leu Gln Arg Gln Ser Pro Glu His Asn Leu Thr His Pro	435 440 445	Glu Leu Ser Val Ala Val Glu Met Leu Ser Ser Val Ala Leu Ile Asn	20 450 455 460	Arg Ala Leu Glu Ser Gly Asp Val Asn Thr Val Trp Lys Gln Leu Ser	465 470 . 475 480	Ser Ser Val Thr Gly Leu Thr Agn Ile Glu Glu Glu Agn Cyg Gln Arg	-485 . 490 495
7O 2004/055519 85/335 85/335 TTEP2003/014057 Thr Asp Asn Val Ile Gln Trp Leu Asn Ala Met Asp Glu Ile Gly Leu		Pro Lys lle Phe Tyr Pro Glu Thr Thr Asp lle Tyr Asp Arg Lys Asn		Met Pro Arg Cys Ile Tyr Cys Ile His Ala Leu Ser Leu Tyr Leu Phe	160	Lys Leu Gly Leu Ala Pro Gln Ile Gln Asp Leu Tyr Gly Lys Val Asp	175	Phe Thr Glu Glu Ile Asn Asn Met Lys Thr Glu Leu Glu Lys Tyr	190	Gly 11e Gln Met Pro Ala Phe Ser Lys 11e Gly Gly 11e Leu Ala Asn	205	Glu Leu Ser Val Asp Glu Ala Ala Leu His Ala Ala Val Ile Ala Ile		Asn Glu Ala Ile Asp Arg Arg Ile Pro Ala Asp Thr Phe Ala Ala Leu	240	Lys Asn Pro Asn Ala Met Leu Val Asn Leu Glu Glu Pro Leu Ala Ser	255	Thr Tyr Gln Asp Ile Leu Tyr Gln Ala Lys Gln Asp Lys Met Thr Asn	270	Ala Lys Asn Arg Thr Glu Asn Ser Glu Arg Glu Arg Asp Val Tyr Glu	285	Glu Leu Leu Thr Gln Ala Glu Ile Gln Gly Asn Ile Asn Lys Val Asn	

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Tyr Leu Asp Glu Leu Met Lys Leu Lys Ala Gln Ala His Ala Glu Asn		Trp Val Lys Gly	Trp Val Lys Gly Gly Tyr Tyr Tyr His Asn Ley Glu Thr Gln Glu	Ley Glu Thr Gln Glu
500 505 510		069	695	700
Asn Glu Phe Ile Thr Trp Asn Asp Ile Gln Ala Cys Val Asp His Val		Gly Gly Trp Asp	Gly Gly Trp Asp Glu Pro Pro Asn Phe Val Gln Asn Ser Met Gln Leu	Asn Ser Met Gln Leu
515 520 525		. 705	710. 715	720
Asn Leu Vel Val Gln Glu His Glu Arg Ile Leu Ala Ile Gly Leu		5 Ser Arg Glu Glu	Ser Arg Glu Glu 11e Gln Ser Ser Gly Val Thr Ala Ala Tyr	Val Thr Ala Ala Tyr
530 535 540			725 730	735
Ile Asn Glu Ala Leu Asp Glu Gly Asp Ala Gln Lys Thr Leu Gln Ala		Asn Arg Glu Gln	Asn Arg Glu Gln Leu Trp Leu Ala Asn Glu Gly Leu Ile Thr Arg Leu	Leu Ile Thr Arg Leu
545 550 550		740	745	750
Leu Gin ile Pro Ala Ala Lys Leu Giu Giy Val Leu Ala Giu Val Ala		Gln Ala Arg Cys	Gin Ala Arg Cys Arg Gly Tyr Leu Vel Arg Gin Glu Phe Arg Ser Arg	Glu Phe Arg Ser Arg
565 570 575		10 755	760	765
Gln His Tyr Gln Asp Thr Leu Ile Arg Ala Lys Arg Glu Lys Ala Gln		Met Asn Phe Leu	Met Asn Phe Leu Lys Lys Gln Ile Pro Ala Ile Thr Cys Ile Gln Ser	Thr Cys Ile Gln Ser
580 585 590		770	775	780 ·
Glu ile Gin Asp Glu Ser Ala Val Leu Trp Leu Asp Glu ile Gln Gly		Gln Trp Arg Gly	Gln Trp Arg Gly Tyr Lys Gln Lys Lys Ala Tyr Gln Asp Arg Leu Ala	Gln Asp Arg Leu Ala
595 600 605	,	785	790 795	. 008
Gly ile Trp Gin Ser Asn Lys Asp Thr Gin Glu Ala Gin Lys Phe Ala		15 Tyr Leu Arg Ser	Tyr Leu Arg Ser His Lys Asp Glu Val Val Lys Ile Gln Ser Leu Ala	Ile Gln Ser Leu Ala
610 615 620			805 810	815
Leu Gly Ile Phe Ala Ile Asn Glu Ala Val Glu Ser Gly Asp Val Gly	٠	Arg Met His Gln	Arg Met His Gin Ala Arg Lys Arg Tyr Arg Asp Arg Leu Gin Tyr Phe	Arg Leu Gln Tyr Phe
625 630 635 640		. 820	825	830
Lys Thr Leu Ser Ala Leu Arg Ser Pro Asp Val Gly Leu Tyr Gly Val		Arg Asp His Ile	Arg Asp His Ile Asn Asp Ile Ile Lys Ile Gin Ala Phe Ile Arg Ala	Ala Phe Ile Arg Ala
645 · 650 · 655		20 835	840	845
lle Pro Glu Cys Gly Glu Thr Tyr His Ser Asp Leu Ala Glu Ala Lys		Asn Lys Ala Arg	Asn Lys Ala Arg Asp Asp Tyr Lys Thr Leu Ile Asn Ala Glu Asp Pro	Asn Ala Glu Asp Pro
660 665 670		850	855	860
Lys Lys Leu Ala Val Gly Asp Asn Asn Ser Lys Trp Val Lys His		Pro Met Val Val	Pro Met Val Val Val Arg Lys Phe Val His Leu Leu Asp Gln Ser Asp	Leu Asp Gln Ser Asp
675 680 · 685			870 875	880

	WO 2004/055519	89/335	PCT/EP2003/014057		WO 2004/055519	90/335	PCT/EP2003/014057
	Gln Asp Phe G	Gln Asp Phe Gln Glu Glu Leu Asp Leu Met Lys Met Arg	t Arg Glu Glu Val		Arg Gln Ile Leu Ala Pro	Arg Gin ile Leu Ala Pro Val Val Lys Glu ile Met Asp Asp Lys	Авр Авр Гув
		885 890	895		1070	1075 1080	
	Ile Thr Leu I	ile thr Leu ile Arg Ser Asn Gln Gln Leu Glu Asn Asp	n Asp Leu Asn Leu		Ser Leu Asn Ile Lys Thr	Ser Leu Asn Ile Lys Thr Asp Pro Val Asp Ile Tyr Lys Ser Trp	Lys Ser Trp
	σ,	. 506 006	910		1085	1090 1095	
N.		Met Asp ile Lys ile Gly Leu Leu Val Lys Asn Lys Ile	s Ile Thr Leu Gln	50	Val Asn Gln Met Glu Ser	Val Asn Gln Met Glu Ser Gln Thr Gly Glu Ala Ser	Lys Leu Pro
	915	920	925		1100	1105 1110	
	Asp val val S	Asp Val Val Ser His Ser Lys Lys Leu Thr Lys Lys Asn	s Asn Lys Glu Gln		Tyr Asp Val Thr Pro Glu	Tyr Asp Val Thr Pro Glu Gln Ala Leu Ala His Glu	Glu Val Lys
	930	935 940			1115	1120	
	Leu Ser Asp M	Leu Ser Asp Met Met Ile Abn Lys Gln Lys Gly Gly	y Gly Leu Lys Ala		Thr Arg Leu Asp Ser Ser	Thr Arg Leu Asp Ser Ser Ile Arg Asn Met Arg Ala	Val Thr Asp
10	945	950	096	01	1130	1135 1140	
	Leu Ser Lys G	Leu Ser Lys Glu Lys Arg Glu Lys Leu Glu Ala Tyr Gln	r Gin His Leu Phe		Lys Phe Leu Ser Ala Ile Val	Ser Ser Val Asp Lys	ile Pro Tyr
		965 970	975	•	1145	1150 1155	
	Tyr beu beu G	Tyr Leu Leu Gln Thr Asn Pro Thr Tyr Leu Ala Lys Leu	s Leu Ile Phe Gln		Gly Met Arg Phe Ile Ala	Gly Met Arg Phe Ile Ala Lys Val Leu Lys Asp Ser	Leu His Glu
	o,	. 586 086	066	. •	1160	1165 1170	
15		Met Pro Gln Asn Lys Ser Thr Lys Phe Met Asp Ser Val	er Val Ile Phe Thr	15	Lys Phe Pro Asp Ala Gly	Lys Phe Pro Asp Ala Gly Glu Asp Glu Leu Leu Lys	Ile Ile Gly
	566	1000	1005		1175	1180 1185	
	Leu Tyr Asn	Leu Tyr Asn Tyr Ala Ser Asn Gln Arg Glu Glu Tyr	Tyr Leu Leu		Asn Leu Leu Tyr Tyr Arg	Asn Leu Leu Tyr Tyr Arg Tyr Met Asn Pro Ala Ile Val Ala Pro	Val Ala Pro
	1010	1015	1020		1190	1195 1200	
	Arg Leu Phe	Arg Leu Phe Lys Thr Ala Leu Gln Glu Glu Ile Lys	Lys Ser Lys Val		Asp Ala Phe Asp Ile Ile	Asp Ala Phe Asp Ile Ile Asp Leu Ser Ala Gly Gly	Gln Leu Thr
20	1025	1030	1035	- 20	1205	1210 1215	
	Asp Gln Ile	Asp Gln Ile Gln Glu Ile Val Thr Gly Asn Pro Thr	Thr Val Ile Lys		Thr Asp Gln Arg Arg Asn	Thr Asp Gln Arg Arg Asn Leu Gly Ser Ile Ala Lys Met Leu Gln	Met Leu Gln
	1040	1045	1050		1220	1225 1230	
	Met Val Val	Met Val Val Ser Phe Asn Arg Gly Ala Arg Gly Gln	Gln Asn Ala Leu	-	His Ala Ala Ser Asn Lys	His Ala Ala Ser Asn Lys Met Phe Leu Gly Asp Asn Ala His Leu	Ala His Leu
	1055	1060	1065		1235	1240 1245	

	WO 2004/055519		91/335	PCT/EP2003/014057	WO 2004/055519	PCT/EP2003/014057
	Ser 11e		Ile Asn Glu Tyr Leu Ser Gln Ser Tyr Gln	Lys Phe Arg	Ile Arg Asp Ale Lys Thr Pro Asp Lys Met Lys Lys	o Asp Lys Met Lys Lys Ser Lys Ser
	1250	1255	5 1260		1430 14	1435 1440
	Arg Phe		Phe Gin Thr Ala Cys Asp Val Pro Glu Leu	Gln Asp Lys	Val Lys Glu Asp Ser Asn Le	Glu Asp Ser Asn Leu Thr Leu Gln Glu Lys Lys Glu Lys
	1265	1270	1275		1445	50 1455
ī,		Val Asp Glu Tyr Ser	Phe Asn Val Asp Glu Tyr Ser Asp Leu Val Thr Leu	Thr Lys Pro	5 Ile Gln Thr Gly beu Lys Ly	Thr Gly Leu Lys Lys Leu Thr Glu Leu Gly Thr Val Asp
	1280	1285	5 1290		1460 1465	65 1470
	Val Ile	Tyr lle Ser Ile Gly	Glu Ile Ile Asn Thr	His Thr Leu	Pro Lys Asn Lys Tyr Gln Gl	Pro Lys Asn Lys Tyr Gln Glu Leu Ile Asn Asp Ile Ala Arg Asp
	1295	1300	1305		1475 1480	80 1485
	ren ren	Asp His Gln Asp Ala	Leu Leu Asp His Gln Asp Ala Ile Ala Pro Glu His	Asn Asp Pro	ile Arg Asn Gin Arg Arg Ty	Asn Gin Arg Arg Tyr Arg Gin Arg Arg Lys Ale Glu Leu
9	1310	1315	1320.		10. 1490 1495	95 1500
	Ile His		Glu Leu Leu Asp Asp Leu Gly Glu Val Pro	Thr Ile Glu	Val Lys Leu Gln Gln Thr Tyr	r Ala Ala Leu Aen Ser Lye Ala Thr
	1325	1330	1335		1505 1510	10 1515
	Ser Leu		lle Gly Glu Ser Ser Gly Asn Leu Asn Asp	Pro Asn Lys	Phe Tyr Gly Glu Gln Val Asp	p Tyr Tyr Lys Ser Tyr Ile Lys Thr
	1340	1345	1350		1520 1525	25 1530
15		Leu Ala Lys Thr Glu	Glu Ala Leu Ala Lys Thr Glu Val Ser Leu Thr Leu	Thr Asn Lys	15 Cys Leu Asp Asn Leu Ala Ser Lys Gly Lys Val Ser	r Lys Gly Lys Val Ser Lys Lys Pro
	1355	1360	1365		1535 1540	40 1545
	Phe Asp	Val Pro Gly Asp Glu	Phe Asp Val Pro Gly Asp Glu Asn Ala Glu Met Asp	Ala Arg Thr	Arg Glu Met Lys Gly Lys Lys	s Ser Lys Lys Ile Ser Lau Lys Tyr
	1370	1375	1380		1550 1555	55 1560
	Ile Leu	ile Leu Leu Asn Thr Lys Arg Leu Ile Val Asp Val		Ile Arg Phe	Thr Ala Ala Arg Leu His Glu	. Lys Gly Val Leu Leu Glu Ile Glu
20	1385	1390	1395	•	20 1565 1570	70 1575
	Gln Pro	Gln Pro Gly Glu Thr Leu Thr Glu Ile Leu Glu Thr		Pro Ala Thr	Asp Leu Gln Val Asn Gln Pho	Gln Val Asn Gin Phe Lys Asn Val Ile Phe Glu Ile Ser
	1400	1405	1410		1580 1585	1590
	Ser Glu	Gln Glu Ala Glu His	Ser Glu Gln Glu Ala Glu His Gln Arg Ala Met Gln Ar	urg Arg Ala	Pro Thr Glu Glu Val Gly Asp	Phe Glu Val Lys Ala Lys Phe Met
	1415	1420	1425		1595 1600	1605

Gly Val Gln Met Glu Thr Phe Met Leu His Tyr Gln Asp Leu Leu 1610 1615	WO 2004/055519 PCT/RP2003/014057
1610 1615 1620	20 25 30
	Glu Leu Asn Asp Leu Phe Lys Ala Ala Cys Leu Pro Leu Pro Gly Tyr
Gln Leu Gln Tyr Glu Gly Val Ala Val Met Lys Leu Phe Asp Arg	35 40 . 45
1625 1630 1635	Arg Val Arg Glu Ile Thr Glu Asn Leu Met Ala Thr Gly Asp Leu Asp
5 Ala Lys Val Asn Val Asn Leu Leu Ile Phe Leu Leu Asn Lys Lys	5 50 55 60
1640 1645 1650	Gin Asp Gly Arg ile Ser Phe Asp Glu Phe ile Lys ile Phe His Gly
Phe Tyr Gly Lys	65 70 75 80
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	56 06
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<212> PRT	115 120 125
<213> Homo sapiens	Trp Ile Asn Lys Ala Leu Glu Asn Asp Pro Asp Cys Arg His Val Ile
15 <220>	15 130 135 140
<221> L-plastin (Lymphocyte cytosolic protein 1)	. Pro Met Asn Pro Asn Thr Asn Asp Leu Phe Asn Ala Val Gly Asp Gly
<222> (1)(627)	145 150 155 160
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Met Ala Arg Gly Ser Val Ser Asp Glu Glu Met Met Glu Leu Arg Glu	Asn Leu Asn Leu Ala Leu Asn Ser Ala Ser Ala Ile Gly Cys His Val
1 5 10 . 15	200 205
Ala Phe Ala Lys Val Asp Thr Asp Gly Asn Gly Tyr Ile Ser Phe Asn	Val Asn Ile Gly Ala Glu Asp Leu Lys Glu Gly Lys Pro Tyr Leu Val

_	WO 2004/055519		PCT/FP2003/014057	OFFENDER OFFE	
		95/335			PC1/EP2003/014057
	210	215	220	405 410	415
	Leu Gly Leu Leu Trp Gln Val 11e Lys 11e Gly Leu Phe	Val lle Lys lle G	Gly Leu Phe Ala Asp Ile	Tyr Ser Asp Leu Ser Asp Ala Leu Val Ile Phe Gln Leu Tyr Glu Lys	Glu Lys
	225 230		235 240	420 425 430	
	Glu Leu Ser Arg Asn Glu Ala Leu Ile Ala Leu Leu Arg	Ala Leu Ile Ala L	Leu Leu Arg Glu Gly Glu	lle Lys Val Pro Val Asp Trp Asn Arg Val Asn Lys Pro Pro Tyr Pro	Tyr Pro
S.	245	250	255	5 435 440 445	٠
	Ser Leu Glu Asp Leu Met Lys Leu Ser Pro Glu Glu Leu Leu Leu Arg	Lys Leu Ser Pro G	th Glu Leu Leu Leu Arg	Lys Leu Gly Gly Asn Met Lys Lys Leu Glu Asn Cys Asn Tyr Ala Val	Ala Vel
	260	265	. 270	450 455 460	
	Trp Ala Asn Tyr His Leu Glu Asn Ala Gly Cys Asn Lys Ile Gly Asn	Glu Asn Ala Gly C	ys Asn Lys Ile Gly Asn	Glu Leu Gly Lys Asn Gln Ala Lys Phe Ser Leu Val Gly Ile Gly Gly	Gly Gly
	275	280	285	465 470 475	480
2	Phe Ser Thr Asp Ile Lys Asp Ser Lys Ala Tyr Tyr His Leu Leu Glu	Asp Ser Lys Ala T	Yr Tyr His Leu Leu Glu	10 Gln Asp Leu Asn Glu Gly Asn Arg Thr Leu Thr Leu Ala Leu Ile Trp	Ile Trp
	290	295	300	485 490	495
	Gin Val Ala Pro Lys Gly Asp Glu Glu Gly Val Pro Ala Val Val Ile	Asp Glu Glu Gly V	al Pro Ala Val Val Ile	Gln Leu Met Arg Arg Tyr Thr Leu Asn 11e Leu Glu Glu 11e Gly Gly	Gly Gly
•	305 310	•	315 320	500 505 510	
	Asp Met Ser Gly Leu Arg Glu Lys Asp Asp Ile Gln Arg	Glu Lys Asp Asp I	ile Gln Arg Ala Glu Cys	Gly Gln Lys Val Asn Asp Asp Ile Ile Val Asn Trp Val Asn Glu Thr	Glu Thr
15	. 325	330	335	15 515 520 525	
	Met Leu Gln Gln Ala Glu Arg Leu Gly Cys Arg Gln Phe Val Thr Ala	Arg Leu Gly Cys A	rg Gln Phe Val Thr Ala	Leu Arg Glu Ala Glu Lys Ser Ser Ile Ser Phe Lys Asp Pro	Авр Рго
	340	345	350	530 535 540	
	Thr Asp Val Val Arg Gly Asn Pro Lys Leu Asn Leu Ala Phe Ile Ala	Asn Pro Lys Leu A	en Leu Ala Phe Ile Ala	Lys 11e Ser Thr Ser Leu Pro Val Leu Asp Leu I1e Asp Ale 11e Gln	Ile Gln
	355	360	365	545 550 555	560
50	Asn Leu Phe Asn Arg Tyr Pro Ala Leu His Lys Pro Glu Asn Gln Asp	Pro Ala Leu His L	ys Pro Glu Asn Gln Asp	20 Pro Gly Ser Ile Asn Tyr Asp Leu Leu Lys Thr Glu Asn Leu Asn Asp	Aen Aep
	370	375	380	565 570 5	575
	lle Asp Trp Gly Ala Leu Glu Gly Glu Thr Arg Glu Glu Arg Thr	Glu Gly Glu Thr A.	rg Glu Glu Arg Thr Phe	Asp Glu Lys Leu Asn Asn Ala Lys Tyr Ala Ile Ser Met Ala Arg Lys	Arg Lys
	385 390		395 400	580 585 590	
	Arg Asn Trp Met Asn Ser Leu Gly Vel Asn Pro Arg Vel Asn His Leu	Leu Gly Val Asn P.	ro Arg Val Asn His Leu	Ile Gly Ala Arg Val Tyr Ala Leu Pro Glu Asp Leu Val Glu Val Asn	Val Asn

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595	600 605			55 60	
Pro Lys Met Val Met Thr Val Phe Ala Cys Leu Met Gly		Lys Gly Met	Asp Thr Ala Gly Gln Glu	Asp Thr Ala Gly Gln Glu Lys Phe Gly Gly Leu Arg Asp Gly Tyr Tyr	Tyr Tyr
610 615	620		. 70	. 75	80
Lys Arg Val			ile Gln Ala Gln Cys Ala	ile Gin Ala Gin Cys Ala ile ile Met Phe Asp Val Thr Ser Arg Val	Arg Vel
5 625				06	95
		•	Thr Tyr Lys Asn Val Pro	Thr Tyr Lys Asn Val Pro Asn Trp His Arg Asp Leu Val Arg Val Cys	Val Cys
			100	105	
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<211> 216			115	120 .125	
10 <212> PRT			10 Arg Lys Val Lys Ala Lys	Arg Lys Val Lys Ala Lys Ser Ile Val Phe His Arg Lys Lys Asn Leu	Asn Leu
<213> Homo sapiens	•		130	135 140	
<220>			Gln Tyr Tyr Asp Ile Ser	Gln Tyr Tyr Asp Ile Ser Ala Lys Ser Asn Tyr Asn Phe Glu Lys Pro	Lys Pro
<221> GTP-binding nuclear protein RAN	otein RAN		145 150	155	160
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15 <223> Accession No. as of 09 Dec 2002; P17080	Dec 2002; P17080		15 165	170	175
<400> 27			Val Ala Met Pro Ala Leu	Val Ala Met Pro Ala Leu Ala Pro Pro Glu Val Val Met Amp Pro Ala	Pro Ala
			180	185 190	
Met Ala Ala Gln Gly Glu Pro Gln Val Gln Phe Lys Leu		Val Leu Val	Leu Ala Ala Gln Tyr Glu	Leu Ala Ala Gln Tyr Glu His Asp Leu Glu Val Ala Gln Thr Thr Ala	Thr Ala
1 5	10		195	200 205	
20 Gly Asp Gly Gly Thr Gly Lys Thr Thr Phe Val Lys Arg		His Leu Thr	20 Leu Pro Asp Glu Asp Asp Asp Leu	nen den	
20	25 30		210	215	
Gly Glu Phe Glu Lys Lys Tyr Val Ala Thr Leu Gly Val		Glu Val His			
35 40	0 45		٠		٠.
Pro Leu Val Phe His Thr Asn Arg Gly Pro Ile Lys Phe		Asn Val Trp	<210> 28		

	WO 2004/055519 PCT/EP2003/014057	WO 2004/055519 PCT/RP2003/014057
	99/33\$	100/335
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	<213> Homo sapiens	130 135 140
-	<220>	Cys Glu Leu Arg Leu Leu Ile His Gln Ser Leu Ala Gly Gly Ile Ile
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		180 185 1.90
	10 Met Glu Thr Glu Gln Pro Glu Glu Thr Phe Pro Asn Thr Glu Thr Asn	10 Val Leu Ile Gly Gly Lys Pro Asp Arg Val Val Glu Cys Ile Lys Ile
	1 5 10 15	200 205
	Gly Glu Phe Gly Lys Arg Pro Ala Glu Asp Met Glu Glu Glu Gln Ala	ile Leu Asp Leu ile Ser Glu Ser Pro ile Lys Gly Arg Ala Gln Pro
	20 25 30	210 215 220
	Phe Lys Arg Ser Arg Asn Thr Asp Glu Met Val Glu Leu Arg Ile Leu	Tyr Asp Pro Asn Phe Tyr Asp Glu Thr Tyr Asp Tyr Gly Gly Phe Thr
•	15 35 40 45	15 225 230 235 240
	Leu Gln Ser Lys Asn Ala Gly Ale Val Ile Gly Lys Gly Gly Lys Asn	Met Met Phe Asp Arg Arg Gly Arg Pro Val Gly Phe Pro Met Arg
	. 60	245 250 255
	Ile Lys Ala Leu Arg Thr Asp Tyr Asn Ala Ser Val Ser Val Pro Asp	Gly Arg Gly Gly Phe Asp Arg Met Pro Pro Gly Arg Gly Gly Arg Pro
	65 70 75 80	260 265 270
	20 Ser Ser Gly Pro Glu Arg Ile Leu Ser Ile Ser Ala Asp Ile Glu Thr	20 Met Pro Pro Ser Arg Arg Asp Tyr Asp Asp Met Ser Pro Arg Arg Gly
	96 06 58	275 280 . 285
	ile Gly Glu ile Leu Lys Lys ile ile Pro Thr Leu Glu Glu Gly Leu	Pro Pro Pro Pro Pro Gly Arg Gly Gly Arg Gly Gly Ser Arg Ala
	100 105 110	290 295 300
	Gln Leu Pro Ser Pro Thr Ala Thr Ser Gln Leu Pro Leu Glu Ser Aap	Arg Asn Leu Pro Leu Pro Pro Pro Pro Pro Arg Gly Gly Asp Leu

. .

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130 135 . 140	9 25 60	
Met Val Ala Leu Leu Asp Tyr Arg Glu Asp Gly Val Thr Pro Tyr Met	Lys Asp Ala Gln Glu Lys Leu Glu Leu Ala Glu Lys Lys Ala Thr Asp	
145 150 155 160	65 . 70 75 80	
ile Phe Phe Lys Asp Gly Leu Glu Met Glu Lys Cys	Ala Glu Ala Asp Val Ala Ser Leu Asn Arg Arg Ile Gln Leu Val Glu	
5 165 170		
,	Glu Glu Leu Asp Arg Ala Glu Arg Leu Ala Thr Ala Leu Gln Lys	
	100 105 110	
<210> 30	Leu Glu Glu Ala Glu Lys Ala Ala Asp Glu Ser Glu Arg Gly Met Lys	
<211> 284	115 120 125	
) <212> PRT	10 Val 11e Glu Ser Arg Ala Gln Lys Asp Glu Glu Lys Met Glu 11e Gln	
<213> Homo sapiens	130 135 140	
. <220>	Glu ile Gin Leu Lys Glu Ala Lys His ile Ala Glu Asp Ala Asp Arg	
<221> Tropomyosin 1 alpha chain	145 150 155 160	
<222> (1)(284)	Lys Tyr Glu Glu Val Ala Arg Lys Leu Val Ile Glu Ser Asp Leu	
<223> Accession No. as of 06 Dec 2002: P09493	15 165 170 175	
<400> 30	Glu Arg Ala Glu Glu Arg Ala Glu Leu Ser Glu Gly Lys Cys Ala Glu	
	180 185 190	
Met Asp Ala Ile Lys Lys Lys Met Gin Met Leu Lys Leu Asp Lys Glu	Leu Glu Glu Leu Lys Thr Val Thr Asn Asn Leu Lys Ser Leu Glu	
1 5 10 15	195 200 205	
Asn Ala Leu Asp Arg Ala Glu Gln Ala Glu Ala Asp Lys Lys Ala Ala	20 Ala Gln Ala Glu Lys Tyr Ser Gln Lys Glu Asp Arg Tyr Glu Glu	•
20 25 30	210 215 220	
Glu Asp Arg Ser Lys Gln Leu Glu Asp Glu Leu Val Ser Leu Gln Lys	Ile Lys Val Leu Ser Asp Lys Leu Lys Glu Ala Glu Thr Arg Ala Glu	
35 .40 45	225 230 235 240	
Lys Leu Lys Gly Thr Glu Asp Glu Leu Asp Lys Tyr Ser Glu Ala Leu	Phe Ala Glu Arg Ser Val Thr Lys Leu Glu Lys Ser Ile Asp Asp Leu	

	WO 2004/055519	105/335	PCT/EP2003/014057	WO 2004/055519 PCT/EP2003/014057
-	. 245	. 250	255	25 60
	Glu Asp Glu Leu Tyr	Glu Asp Glu Leu Tyr Ala Gln Lys Leu Lys Tyr Lys Ala	la ile Ser Glu	Ser Ala Gln Gly Ala Gln Ile Gly Ala Met Leu Met Ala Ile Arg Leu
	260	265	270	65 70 75 80
	Glu Leu Asp His Ala	Glu Leu Asp His Ala Leu Asn Asp Met Thr Ser Ile		Arg Gly Met Amp Leu Glu Glu Thr Ser Val Leu Thr Gln Ale Leu Ale
'n	275	. 280		56 06 58 5
				Gin Ser Gly Gin Gin Leu Glu Trp Pro Glu Ala Trp Arg Gin Gin Leu
				100 105 110
	<210> 31	·		Val Asp Lys His Ser Thr Gly Gly Val Gly Asp Lys Val Ser Leu Val
	<211> 482		•	115 120 125
2	<212> PRT			10 Leu Ala Pro Ala Leu Ala Ala Cys Gly Cys Lys Val Pro Met Ile Ser
	<213> Homo sapiens			130 135 140
	<220>			Gly Arg Gly Leu Gly His Thr Gly Gly Thr Leu Asp Lys Leu Glu Ser
	<221> Thymidine ph	Thymidine phosphorylase precursor		145 150 155 160
	<222> (1)(482)			ile Pro Gly Phe Asn Val Ile Gln Ser Pro Glu Gln Met Gln Val Leu
15	<223> Accession No	Accession No. as of 09 Dec 2002; P19971	51	5 165 170 175
	<400> 31			Leu Asp Gln Ala Gly Cys Cys Ile Val Gly Gln Ser Glu Gln Leu Val
				180 185 190
	Met Ala Ala Leu Met	Met Ala Ala Leu Met Thr Pro Gly Thr Gly Ala Pro Pro	to Ala Pro Gly	Pro Ala Asp Gly Ile Leu Tyr Ala Ala Arg Asp Val Thr Ala Thr Val
	1 5	10		195 200 205
70	Asp Phe Ser Gly Glu	Asp Phe Ser Gly Glu Gly Ser Gln Gly Leu Pro Asp Pro	co Ser Pro Glu) Asp Ser Leu Pro Leu lle Thr Ala Ser Ile Leu Ser Lys Lys Leu Val
	20	25	30	210 215 220
	Pro Lys Gln Leu Pro	Pro Lys Gln Leu Pro Glu Leu Ile Arg Met Lys Arg Asp	p Gly Gly Arg	Glu Gly Leu Ser Ala Leu Val Val Asp Val Lys Phe Gly Gly Ala Ala
	35	. 40 45		225 230 235 240 1
	Leu Ser Glu Ala Asp	Leu Ser Glu Ala Asp Ile Arg Gly Phe Val Ala Ala Val	ıl Val Asn Gly	Val Phe Pro Asn Gln Glu Gln Ala Arg Glu Leu Ala Lys Thr Leu Val

	WO 2004/055519	107/335	PCT/EP2003/014057	WO 2004/055519	.108/335	PCT/EP2003/014057
	245	250	. 255	435	440 445	
	Gly Val Gly Ala Ser Leu Gly Leu Arg Val Ala Ala Ala		Leu Thr Ala	Gly Pro Gln Ser Arg Al	Gly Pro Gln Ser Arg Ala Leu Gln Glu Ala Leu Val Leu Ser Asp Arg	der Asp Arg
	260	265	270	450	455 460	
	Met Asp Lys Pro Leu Gly Arg Cys Val Gly His Ala Leu		Glu Val Glu	Ala Pro Phe Ala Ala Pr	Ala Pro Phe Ala Ala Pro Leu Pro Phe Ala Glu Leu Val Leu Pro Pro	eu Pro Pro
	5 275 . 280	80 285		5 465 . 470	475	480
	Glu Ala Leu Leu Cys Met Asp Gly Ala Gly Pro Pro Asp	ly Ala Gly Pro Pro Asp	Leu Arg Asp	Gln Gln		
	290 295	300				
	Leu Val Thr Thr Leu Gly Gly Ala Leu Leu Trp Leu Ser		Gly His Ala			
	305 310	315	320			
9	Gly Thr Gln Ala Gln Gly Ala Ala Arg Val Ala Ala Ala		Leu Asp Asp	10 <210> 32		
	325	330	335	<211> 488		
	Gly Ser Ala Leu Gly Arg Phe Glu Arg Met Leu Ala Ala		Gln Gly Val	<212> PŘT		
	340	345	350	<213> Homo sapiens		
	Asp Pro Gly Leu Ala Arg Ala Leu Cys Ser Gly Ser Pro		Ala Glu Arg	<220>		
15	355 . 360	365		15 <221> Cytosol aminopeptidase	tidase	-
	Arg Gln Leu Leu Pro Arg Ala Arg Glu Glu Glu Leu Leu Ala Pro	g Glu Gln Glu Glu Leu I	eu Ala Pro	<222> (1) (488)		
	376 375	380		<223> Accession No. as	Accession No. as of 09 Dec 2002: P28838	
	Ala Asp Gly Thr Val Glu Leu Val Arg Ala Leu Pro Leu Ala Leu Val	l Arg Ala beu Pro beu A	la Leu Val	<400> 32		
	385 390	395	400	٠		
70	Leu His Glu Leu Gly Ala Gly Arg Ser Arg Ala Gly	Glu	Pro Leu Arg	20 Met Thr Lys Gly Leu Val	Met Thr Lys Gly Leu Val Leu Gly Ile Tyr Ser Lys Glu Lys Glu Asp	ra Glu Asp
	405	410	415	1	10	15
	Leu Gly Val Gly Ala Glu Leu Leu Val Asp Val Gly Gln Arg Leu Arg	ı Val Asp Val Gly Gln A	rg beu Arg	Asp Val Pro Gln Phe Thr	Asp Val Pro Gin Phe Thr Ser Ala Gly Glu Asn Phe Asp Lys Leu Leu	rs Leu Leu
	420	425	430	30	25 30	
	Arg Gly Thr Pro Trp Leu Arg Val His Arg Asp Gly Pro Ala Leu Ser	l His Arg Asp Gly Pro A	la Leu Ser	Ala Gly Lys Leu Arg Glu	Ala Gly Lys Leu Arg Glu Thr Leu Asn 11e Ser Gly Pro Pro Leu Lys	o Leu Lys

WO 2004/055519 PCT/EP2003/014057	225 230 235 240	Ala Asn Glu Pro Pro Leu Val Phe Val Gly Lys Gly Ile Thr Phe Asp	245 250 255	Ser Gly Gly Ile Ser Ile Lys Ala Ser Ala Asn Met Asp Leu Met Arg	5 260 265 270 .	Ala Asp Met Gly Gly Ala Ala Thr Ile Cys Ser Ala Ile Val Ser Ala	275 280 285	Ala Lys Leu Asn Leu Pro Ile Asn Ile Ile Gly Leu Ala Pro Leu Cys	290 295 . 300	10 Glu Asn Met Pro Ser Gly Lys Ala Asn Lys Pro Gly Asp Val Val Arg	305 310 315 320	Ala Lys Asn Gly Lys Thr Ile Gin Val Asp Asn Thr Asp Ala Glu Gly	325 330 335	Arg Leu Ile Leu Ala Asp Ala Leu Cys Tyr Ala His Thr Phe Asn Pro	15 340 345 350	Lys Val 11e Leu Asn Ala Ala Thr Leu Thr Gly Ala Met Asp Val Ala	355 360 365	Leu Gly Ser Gly Ala Thr Gly Val Phe Thr Asn Ser Ser Trp Leu Trp	370 375 380	20 Asn Lys Leu Phe Glu Ala Ser Ile Glu Thr Gly Asp Arg Val Trp Arg	385 390 395 400	Met Pro Leu Phe Glu His Tyr Thr Arg Gln Val Val Asp Cys Gln Leu	405 410 . 415	Ala Asp Val Asn Asn Ile Gly Lys Tyr Arg Ser Ala Gly Ala Cys Thr
WO 2004/055519 PCT/EP2003/014057 109/335	35 40 45	Ala Gly Lys Thr Arg Thr Phe Tyr Gly Leu His Gln Asp Phe Pro Ser		Val Val Leu Val Gly Leu Gly Lys Lys Ala Ala Gly Ile Asp Glu Gln	5 65 70 75 80	Glu Asn Trp His Glu Gly Lys Glu Asn Ile Arg Ala Ala Val Ala Ala	. 85 90 95	Gly Cys Arg Gln Ile Gln Asp Leu Glu Leu Ser Ser Val Glu Val Asp	100 105 110	10 Pro Cys Gly Asp Ala Gln Ala Ala Ala Glu Gly Ala Val Leu Gly Leu	115 120 125	Tyr Glu Tyr Asp Asp Leu Lys Gln Lys Lys Lys Met Ala Val Ser Ala	130 135 140	Lys Leu Tyr Gly Ser Gly Asp Gln Glu Ala Trp Gln Lys Gly Val Leu	15 145 150 155 160	Phe Ala Ser Gly Gln Asn Leu Ala Arg Gln Leu Met Glu Thr Pro Ala	165 170 175	Asn Glu Met Thr Pro Thr Arg Phe Ala Glu Ile Ile Glu Lys Asn Leu	180 . 185 190	20 Lys Ser Ala Ser Ser Lys Thr Glu Val His Ile Arg Pro Lys Ser Trp	195 200 205	Ile Glu Glu Gln Ala Met Gly Ser Phe Leu Ser Val Ala Lys Gly Ser	210 215 220	Asp Glu Pro Pro Val Phe Leu Glu Ila His Tyr Lys Gly Ser Pro Asn

	WO 2004/055519	44.02.E	PCT/EP2003/014057		,	WO 2004/055519		PCT/EP2003/014057
		111/333					112/335	
	420	425	430			Gly Leu Gly Gly Ser Val Arg Phe Gly Pro Gly Val Ala Phe Arg	Arg Phe Gly Pro Gly Val	Ala Phe Arg
	Ala Ala Ala Phe Leu Lys Glu Phe Val Thr His Pro Lys	he Val Thr His Pro Ly	78 Trp Ala His			20	25	30
	435 4	440 445	.5	·		Ala Pro Ser Ile His Gly Gly Ser Gly Gly Arg Gly Val Ser Val Ser	Ser Gly Gly Arg Gly Val	Ser Val Ser
	Leu Asp Ile Ala Gly Val Met Thr Asn Lys Asp Glu Val	hr Asn Lys Asp Glu Va	al Pro Tyr Leu			. 38	40 45	
5	450 455	460			'n	Ser Ala Arg Phe Val Ser Ser Ser Ser Gly Gly Tyr Gly Gly Gly	Ser Ser Ser Gly Gly Tyr	Gly Gly Gly
	Arg Lys Gly Met Thr Gly Arg Pro Thr Arg Thr Leu Ile	ro Thr Arg Thr Leu Il.	e Glu Phe Leu			50 55		
	465 470	475	480			Tyr Gly Gly Val Leu Thr Ala Ser Asp Gly Leu Leu Ala Gly Asn Glu	Ser Asp Gly Leu Leu Ala	Gly Asn Glu
	Leu Arg Phe Ser Gln Asp Asn Ala	1.0				65 70	75	80
	485			•	:	Lys Leu Thr Met Gln Asn Leu Asp Arg Leu Ala Ser Tyr Leu Asp	Asn Asp Arg Leu Ala Ser	Tyr Leu Asp
9					10	8	06	95
					•	Lys Val Arg Ala Leu Glu Ala Ala Asn Gly Glu Leu Glu Val Lys Ile	Ala Asn Gly Glu Leu Glu	Val Lys Ile
	<210> 33		·		•	100	.105	110
	<211> 400		,			Arg Asp Try Tyr Gln Lys Gln Gly Pro Gly Pro Ser Arg Asp Tyr Ser	Gly Pro Gly Pro Ser Arg	Asp Tyr Ser
	<212> PRT					115	120 . 125	
15	<213> Homo sapiens				15	His Tyr Tyr Thr The Gln Asp Leu Arg Asp Lys Ile Leu Gly Ala	Asp Leu Arg Asp Lys Ile	Leu Gly Ala
	<2220>					130 135	140	
	<221> Keratin, type I cytoskeletal 19	iletal 19			•	Thr Ile Glu Asn Ser Arg Ile Val Leu Gln Ile Asp Asn Ale Arg Leu	Val Leu Gln Ile Asp Asn	Ala Arg Leu
	<222> (1)(400)			•		145 . 150	155	. 160
	<223> Accession No. as of 09 Dec 2002 : P08727	Dec 2002 : P08727				Ala Ala Asp Asp Phe Arg Thr Lys Phe Glu Thr Glu Gln Ala Leu Arg	Lys Phe Glu Thr Glu Gln	Ala Leu Arg
70					20	165	170	175
	<400> 33					Met Ser Val Glu Ala Asp Ile Asn Gly Leu Arg Arg Val Leu Asp Glu	Asn Gly Leu Arg Arg Val	Leu Asp Glu
						180	185	190
	Met Thr Ser Tyr Ser Tyr Arg Gln Ser Ser Ala Thr Ser	n Ser Ser Ala Thr. Ser	r Ser Phe Gly	•		Leu Thr Leu Ala Arg Thr Asp Leu Glu Met Gln Ile Glu Gly Leu Lys	Leu Glu Met Gln Ile Glu	3ly Leu Lys
		10	15		•	195	200 205	

-	WO 2004/055519	113/335	PCT/EP2003/014057	WO 2004/055519 Pr 114/335	PCT/EP2003/0
	Glu Glu Leu Ala Tyr Leu Lys Lys Asn His Glu	Lys Lys Asn His Glu Glu Glu Ile Ser Thr	e Ser Thr		
	210	215 220			
	Leu Arg Gly Gln Val Gly Gly Gln Val Ser Val	. Gly Gln Val Ser Val Glu Val Asp Ser Ala	p Ser Ala	<210> 34	
	225 230	235	240	<211> 325	
·	Pro Gly Thr Asp Leu Ala	Pro Gly Thr Asp Leu Ala Lys Ile Leu Ser Asp Met Arg Ser Gln Tyr	r Gln Tyr	<212> PRT	•
	245	250	255	<213> Homo sapiens	
	Glu Val Met Ala Glu Gln	Glu Val Met Ala Glu Gln Asn Arg Lys Asp Ala Glu Ala Trp Phe Thr) Phe Thr	<2220>	•
	260	265 270		<221> Alcohol dehydrogenase [NADP+]	
	Ser Arg Thr Glu Glu Leu	Ser Arg Thr Glu Glu Leu Asn Arg Glu Val Ala Gly His Thr Glu Gln	r Glu Gln	<222> (1)(325)	
91	275	280 285	01	<223> Accession No. as of 09 Dec 2002; P14550	
	Leu Gln Met Ser Arg Ser	Leu Gln Met Ser Arg Ser Glu Val Thr Asp Leu Arg Arg Thr Leu Gln	r Leu Gln	<400> 34	
	290	300			
	Gly Leu Glu Ile Glu Leu	Gly Leu Glu Leu Glu Leu Gln Ser Gln Leu Ser Met Lys Ala Ala Leu	Ala Leu	Met Ala Ala Ser Cys Val Leu Leu His Thr Gly Gln Lys Met Pro Leu	Pro Leu
	305 . 310	315	320	1 5 10	15
15	Glu Asp Thr Leu Ala Glu	Glu Asp Thr Leu Ala Glu Thr Glu Ala Arg Phe Gly Ala Gln Leu Ala	n Leu Ala	lle Gly Leu Gly Thr Trp Lys Ser Glu Pro Gly Gln Val Lys Ala Ala	Ala Ala
	325	330	. 335	20 25 30	
	His Ile Gln Ala Leu Ile	His Ile Gln Ala Leu Ile Ser Gly Ile Glu Ala Gln Leu Ala Asp Val	a Asp Val	Val Lys Tyr Ala Leu Ser Val Gly Tyr Arg His Ile Asp Cys Ala Ala	Ala Ala
	340	345 350		35 40 45	
	Arg Ala Asp Ser Glu Arg	Arg Ala Asp Ser Glu Arg Gln Asn Gln Glu Tyr Gln Arg Leu Met Asp	1 Met Asp	Ile Tyr Gly Asn Glu Pro Glu Ile Gly Glu Ala Leu Lys Glu Asp Val	Авр Val
20	355	360 365		50 55 60	
	Ile Lys Ser Arg Leu Glu	Ile Lys Ser Arg Leu Glu Gln Glu Ile Ala Thr Tyr Arg Ser Leu Leu	: Leu Leu	Gly Pro Gly Lys Ala Val Pro Arg Glu Glu Leu Phe Val Thr Ser Lys	Ser Lys
	370	375 380		65 70 75	80
	Glu Gly Gln Glu Asp His	Glu Gly Gln Glu Asp His Tyr Asn Asn Leu Ser Ala Ser Lys Val	.Val Leu	Leu Trp Asn Thr Lys His His Pro Glu Asp Val Glu Pro Ala Leu Arg	Leu Arg
	385 . 390	. 395	400	85	95

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WO 2004/055519 PCT/EP2003/014057 115/335	WO 2004/055519 PCT/EP2003/014
	116/335
Lys Thr Leu Ala Asp beu Gln Leu Glu Tyr Leu Asp Leu Tyr Leu Met	Leu Asn Ala Leu Asn Lys Asn Trp Arg Tyr Ile Val Pro Met Leu Thr
100 105 110	290 295 300
His Trp Pro Tyr Ala Phe Glu Arg Gly Asp Asn Pro Phe Pro Lys Asn.	Val Asp Gly Lys Arg Val Pro Arg Asp Ala Gly His Pro Leu Tyr Pro
115 120 125	305 310 315 320
Ale Asp Gly Thr Ile Cys Tyr Asp Ser Thr His Tyr Lys Glu Thr Trp	5 Phe Asn Asp Pro Tyr
130 135 140	325
Lys Ala Leu Glu Ala Leu Val Ala Lys Gly Leu Val Gln Ala Leu Gly	
145 150 . 155 160	
Leu Ser Asn Phe Asn Ser Arg Gln lle Asp Asp lle Leu Ser Val Ala	<210> 35
165 170 175	10 <211> 270
Ser Val Arg Pro Ala Val Leu Gln Val Glu Cys His Pro Tyr Leu Ala	<212> PRT
. 180 185 190	<213> Homo sapiens
Gln Asn Glu Leu Ile Ala His Cys Gln Ala Arg Gly Leu Glu Val Thr	. <220>
195 200 205	<221> Elastase IIIA precursor
Gly Ser Ser Asp Arg A	15 <222> (1) (270)
210 215 220	<223> Accession No. as of 09 Dec 2002: p09093
Glu Pro Val Leu Leu Glu Glu Pro Val Val Leu Ala Leu Ala Glu Lys	<400> 35
225 . 230 235 240	
Tyr Gly Arg Ser Pro Ala Gln Ile Leu Leu Arg Trp Gln Val Gln Arg	Met Met Leu Arg Leu Leu Ser Ser Leu Leu Val Ala Val Ala Ser
245 250 . 255	20 1 5 10 15
Lys Vel 11e Cys 11e Pro Lys Ser 11e Thr Pro Ser Arg 11e Leu Gln	Gly Tyr Gly Pro Pro Ser Ser His Ser Ser Arg Val Val His Gly
260 265 . 270	20 25 30
Asn lle Lys Val Phe Asp Phe Thr Phe Ser Pro Glu Glu Met Lys Gln	Glu Asp Ala Val Pro Tyr Ser Trp Pro Trp Gln Val Ser Leu Gln Tyr
275 280 285	35 40 45

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WO 2004/055519	PCT/EP2003/014057	WO 2004/055519 PC	PCT/EP2003/014057
. 117/335		118/335	
Glu Lys Ser Gly Ser Phe Tyr His Thr Cys Gly Gly Ser	Ser Leu Ile Ala	Gly Phe Gly Cys Asn Phe Ile Arp Lys Pro Thr Val Phe Thr Arg Val	Arg Val
50 55 60		245 250 2:	255
Pro Amp Trp Val Val Thr Ala Gly His Cys Ile Ser Arg	Arg Asp Leu Thr	Ser Ala Phe Ile Asp Trp Ile Glu Glu Thr Ile Ala Ser His	
65 70 75	. 08	260 265 270	
Tyr Gln Val Val Leu Gly Glu Tyr Asn Leu Ala Val Lys	Lys Glu Gly Pro		
85 90	95		
Glu Gin Val Ile Pro Ile Asn Ser Glu Glu Leu Phe Val	Val His Pro Leu	<210> 36	
100 105	110	<211> 509	
Trp Asn Arg Ser Cys Val Ala Cys Gly Asn Asp Ile Ala	Ala Leu ile Lys	<212> PRT .	
115 120 1	125	10 <213> Номо варіелв	
Leu Ser Arg Ser Ala Gln Leu Gly Asp Ala Val Gln Leu	Leu Ala Ser Leu	<220>	
130 135 140		<221> Dihydrolipoamide dehydrogenase, mitochondrial precursor	ursor
Pro Pro Ala Gly Asp Ile Leu Pro Asn Lys Thr Pro Cys Tyr Ile Thr	Cys Tyr 1le Thr	<222> (1)(509)	
145 . 150 155		<223> Accession No. as of 09 Dec 2002: P09622	
Gly Trp Gly Arg Leu Tyr Thr Asn Gly Pro Leu Pro Asp Lys Leu Gln		15 <400> 36	
165 170	175		
Gin Ala Arg Leu Pro Val Val Asp Tyr Lys His Cys Ser Arg Trp Asn	Ser Arg Trp Asn	Met Gln Ser Trp Ser Arg Val Tyr Cys Ser Leu Ale Lys Arg Gly His	1у нів
180 . 185		1 5 10 15	ĸ
Trp Trp Gly Ser Thr Val Lys Lys Thr Met Val Cys Ala Gly Gly Tyr	ala Gly Gly Tyr	Phe Asn Arg Ile Ser His Gly Leu Gln Gly Leu Ser Ala Val Pro Leu	ro Leu
195 200 3	205	20 20 25 30	
lle Arg Ser Gly Cys Asn Gly Asp Ser Gly Gly Pro Leu Asn Cys Pro	eeu Asn Cys Pro	Arg Thr Tyr Ala Asp Gln Pro Ile Asp Ala Asp Val Thr Val Ile Gly	le Gly
210 215 220		35 40 45	
Thr Glu Asp Gly Gly Trp Gln Val His Gly Val Thr Ser Phe Val Ser	er Phe Val Ser	Ser Gly Pro Gly Gly Tyr Val Ala Ala Ile Lys Ala Ala Gln Leu Gly	eu Gly
225 230 235	240	. 09 25 09 .	

PCT/EP2003/014057	n Glu Thr Leu Gly Gly Thr Cys	. 75 80	Gly Cys Ile Pro Ser Lys Ala Leu Leu Asn Asn Ser His	56 06	Tyr His Met Ala His Gly Thr Asp Phe Ala Ser Arg Gly Ile Glu	105	Glu Val Arg Leu Ann Leu Asp Lys Met Met Glu Gln Lys Ser	125	/ Ile Ala His Leu Phe Lys Gln	140	Gly Lys lle Thr Gly Lys Asn	. 155 160	. Gly Thr Gln Val Ile Asp Thr	170 . 175	Ser Glu Val Thr Pro Phe Pro Gly	190	Ser Sêr Thr Gly Ala Leu Ser	205	Val ile Gly Ala Gly Val ile	220	Arg Leu Gly Ala Asp Val Thr	235 240	Glu Phe Leu Gly His Val Gly Gly Val Gly Ile Asp Met Glu	
WO 2004/055519	Phe Lys Thr Val Cys Ile Glu Lys Asn Glu Thr Leu Gly Gly	. 70	Leu Asn Val Gly Cys Ile Pro Ser	85	5 Tyr Tyr His Met Ala His Gly Thr	100	Met Ser Glu Val Arg Leu Asn Leu	115 120	Thr Ala Val Lys Ala Leu Thr Gly Gly Ile Ala His Leu Phe Lys	10 130 135	Asn Lys Val Val His Val Asn Gly Tyr Gly Lys 1le Thr	145 150	Gln Val Thr Ala Thr Lys Ala Asp Gly Gly Thr Gln Val	165	15 Lys Asn Ile Leu Ile Ala Thr Gly 8	180 185	ile Thr ile Asp Glu Asp Thr ile Val	195 200	Leu Lys Lys Val Pro Glu Lys Met Val Val	20 210 215	Gly Val Glu Leu Gly Ser Val Trp Gln Arg Leu Gly Ala Asp Val	225 230	Ala Val Glu Phe Leu Gly His Val G	•

15 Glu Gly Ile Ile Cys Val Glu Gly Met Ala Gly Gly Ala Val His Ile

Asp Tyr Asn Cys Val Pro Ser Val Ile Tyr Thr His Pro Glu Val Ala

Trp Val Gly Lys Ser Glu Glu Gln Leu Lys Glu Glu Gly Ile Glu Tyr

Lys Val Gly Lys Phe Pro Phe Ala Ala Asn Ser Arg Ala Lys Thr Asn

Ala Asp Thr Asp Gly Met Val Lys Ile Leu Gly Gln Lys Ser Thr Asp

Ile Gly Asp Val Val Ala Gly Pro Met Leu Ala His Lys Ala Glu Asp

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rie Ser Lys Asn Phe Gin Arg lie Leu Gin Lys Gin Gly Phe Lys Phe

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Lys Leu Asn Thr Lys Val Thr Gly Ala Thr Lys Lys Ser Asp Gly Lys

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5 Ile Asp Val Ser Ile Glu Ala Ala Ser Gly Gly Lys Ala Glu Val Ile

Thr Cys Asp Val Leu Leu Val Cys Ile Gly Arg Arg Pro Phe Thr Lys

Asn Leu Gly Leu Glu Glu Leu Gly Ile Glu Leu Asp Pro Arg Gly Arg

lle Pro Val Asn Thr Arg Phe Gln Thr Lys Ile Pro Asn Ile Tyr Ala

WO 2004/055519 PCT/EP2003/014057 121/335	WO 2004/055519 PCT/EP2003/014057 122/335
Arg Val Leu Gly Ala His Ile Leu Gly Pro Gly Ala Gly Glu Met Val	Phe Glu Tyr Ile Ile Ala Glu Lys Arg Gly Lys Asn Asn Thr Val Gly
450 455 460	35 40 45
Asn Glu Ala Ala Leu Ala Leu Glu Tyr Gly Ala Ser Cys Glu Asp Ile	Leu lle Gln Leu Asn Arg Pro Lys Ala Leu Asn Ala Leu Cys Asp Gly
465 470 475 480	55 60
5 Ale Arg Vel Cys His Ala His Pro Thr Leu Ser Glu Ala Phe Arg Glu	5 Leu lle Asp Glu Leu Asn Gln Ala Leu Lys lle Phe Glu Glu Asp Pro
485 490 495	65 70 75 80
Ala Asn Leu Ala Ala Ser Phe Gly Lys Ser Ile Asn Phe	Ala Val Gly Ala Ile Val Leu Thr Gly Gly Asp Lys Ala Phe Ala Ala
. 505 505	85 90 95
	Gly Ala Asp Ile Lys Glu Met Gln Asn Leu Ser Phe Gln Asp Cys Tyr
10	10 100 105 110
<210> 37	Ser Ser Lys Phe Leu Lys His Trp Asp His Leu Thr Gln Val Lys Lys
<211> 290	115 120 125
<212> PRT	Pro Val Ile Ala Ala Val Aen Gly Tyr Ala Phe Gly Gly Gly Glu
<213> Homo sapiens	130 135 140
15 <220>	15 Leu Ala Met Met Cys Asp Ile Ile Tyr Ala Gly Glu Lys Ala Gln Phe
<221> Enoyl-CoA hydratase, mitochondrial precursor	145 150 155 160
<222> (1)(290)	Ala Gin Pro Giu ile Leu ile Gly Thr ile Pro Gly Ala Gly Gly Thr
<223> Accession No. as of 09 Dec 2002; P30084	165 170 175
<400> 37	Gln Arg ieu Thr Arg Ale Vel Gly Lys Ser Leu Ale Met Glu Met Vel
	20 180 185 190
Met Ala Ala Leu Arg Val Leu Leu Ser Cys Ala Arg Gly Pro Leu Arg	Leu Thr Gly Asp Arg Ile Ser Ala Gln Asp Ala Lys Gln Ala Gly Leu
1 5 10 15	200 205
Pro Pro Val Arg Cys Pro Ala Trp Arg Pro Phe Ala Ser Gly Ala Asn	Val Ser Lys Ile Cys Pro Val Glu Thr Leu Val Glu Glu Ala Ile Gln
20 25 30	210 215 220

WO 2004/055519	123/335	PCT/EP2003/014057		WO 2004/055519	124/335	PCT/EP2003/014057
Cys Ala Glu Lys Ile Ala Ser Asn Ser Lys Ile Val Val Al	Ser Aan Ser Lya Ile Val	Val Ala Met Ala		Ala Pro Leu Pro	Ala Pro Leu Pro Gly Leu Ser Ala Pro Gly Arg Leu Phe Asp Gln Arg	Phe Asp Gln Arg
225 230	235	240		20	. 25	30
Lys Glu Ser Val Asn Ala Ala Phe Glu Met Thr Leu Thr Glu Gly Ser	Ala Phe Glu Met Thr Leu	Thr Glu Gly Ser		Phe Gly Glu Gly	Phe Gly Glu Gly Leu Leu Glu Ala Glu Leu Ala Ala Leu Cys Pro Thr	eu Cys Pro Thr
245	250	255		35	40	45
5 Lys Leu Glu Lys Lys Leu Phe Tyr Ser Thr Phe Ala Thr Asp Asp Arg	Phe Tyr Ser Thr Phe Ala	Thr Asp Asp Arg		5 Thr Leu Ala Pro	Thr Leu Ala Pro Tyr Tyr Leu Arg Ala Pro Ser Val Ala Leu Pro Val	da Leu Pro Val
. 260	265	270			. 55	
Lys Glu Gly Met Thr Ala Phe Val Glu Lys Arg Lys Ala Asn Phe Lys	Phe Val Glu Lys Arg Lys	Ala Asn Phe Lys		Ala Gln Val Pro	Ala Gln Val Pro Thr Asp Pro Gly His Phe Ser Val Leu Leu Asp Val	eù Leu Asp Val
275	280	285			. 70	80
Asp Gln			٠	Lys His Phe Ser	Lys His Phe Ser Pro Glu Glu Ile Ala Val Lys Val Val Gly Glu His	al Gly Glu His
10 290				. 01	06 58	95
				Val Glu Val His	Val Glu Val His Ala Arg His Glu Glu Arg Pro Asp Glu His Gly Phe	lu His Gly Phe
				100	105	110
<210> 38				. Val Ala Arg Glu	Val Ala Arg Glu Phe His Arg Arg Tyr Arg Leu Pro Pro Gly Val Asp	ro Gly Val Asp
<211> 160				115	120 12	125
15 <212> PRT		٤		15 Pro Ala Ala Val	Pro Ala Ala Val Thr Ser Ala Leu Ser Pro Glu Gly Val Leu Ser Ile	al Leu Ser Ile
<213> Homo sapiens				130	135 140	
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<221> Heat-shock 20 kDa like-protein p20	like-protein p20			145	150 155	160
<222> (1)(160)						·
20 <223> Accession No. as o	Accession No. as of 09 Dec 2002: 014558			20		
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	٠		-	<211> 151		
Met Glu ile Pro Val Gln Pro Ser Trp Leu Arg Arg	al Gln Pro Ser Trp Leu	Arg Arg Ala Ser		<212> PRT		
1	10	15		<213> Homo sapiens	. sue	

	WO 2004/055519	127/335	PCT/EP2003/014057	. WO 2004/055519 128/335	PCT/EP2003/01
	Ser Gly Trp Ile Leu Ser Lys Ala Lys Asp Asp Thr Asp Asp Glu	rs Ala Lys Lys Asp Asp	Thr Asp Asp Glu	Ser Arg Glu Ile Glu Asp Pro Glu Asp Arg Iye Pro Glu Asp Trp Asp	авр Ттр Авр
	85	06	56	275 280 285	
	ile Ala Lys Tyr Asp Gly Lys Trp Glu Val Glu Glu Met Lys Glu	's Trp Glu Val Glu Glu	Met Lys Glu Ser	Glu Arg Pro Lys lle Pro Asp Pro Glu Ala Val Lys Pro Asp Asp Trp	мр Авр Тгр
	100	105	110	290 295 300	
s.	Lys Leu Pro Gly Asp Lys Gly Leu Val Leu Met Ser Arg Ala Lys His	y Leu Val Leu Met Ser	Arg Ala Lys His	5 Asp Glu Asp Ala Pro Ala Lys Ile Pro Asp Glu Glu Ala Thr Lys Pro	thr Lys Pro
	115	120		305 310 315	320
	His Ala Ile Ser Ala Lys Leu Asn Lys Pro Phe Leu Phe Asp Thr Lys	u Asn Lys Pro Phe Leu	Phe Asp Thr Lys	Glu Gly Trp Leu Asp Asp Glu Pro Glu Tyr Val Pro Asp Pro Asp Ala	ro Asp Ala
	130 135	5 140		325 330	335
	Pro Leu Ile Val Gin Tyr Giu Val Asn Phe Gin Asn Gly Ile Giu Cys	u Val Asn Phe Gln Asn	Gly ile Glu Cys	Glu Lys Pro Glu Asp Trp Asp Glu Asp Met Asp Gly Glu Trp Glu Ala	rp Glu Ala
9	145	155	160	10 . 340 345	350
	Gly Gly Ala Tyr Val Lys Leu Leu Ser Lys Thr Pro Glu Leu Asn Leu	u Leu Ser Lys Thr Pro	Glu Leu Asn Leu	Pro Gln Ile Ala Asn Pro Arg Cys Glu Ser Ala Pro Gly Cys Gly Val	ys Gly Val
	165	170	175	355 360 365	
	Asp Gln Phe His Asp Lys Thr Pro Tyr Thr Ile Met Phe Gly Pro Asp	r Pro Tyr Thr Ile Met	Phe Gly Pro Asp	Trp Gln Arg Pro Val 11e Asp Asn Pro Asn Tyr Lys Gly Lys Trp Lys	VS TYP Lys
	180	185	190	370 375 380	
15	Lys Cys Gly Glu Asp Tyr Lys Leu His Phe Ile Phe Arg His Lys Asn	s Leu His Phe Ile Phe	Arg His Lys Asn	15 Pro Pro Met 11e Asp Asn Pro Ser Tyr Gln Gly 11e Trp Lys Pro Arg	/8 Pro Arg
	195	200	205	385 . 390 . 395	400
	Pro Lys Thr Gly Ile Tyr Glu Glu Lys His. Ala Lys Arg Pro Asp Ala	u Glu Lys His.Ala Lys	Arg Pro Asp Ala	Lys Ile Pro Asn Pro Asp Phe Phe Glu Asp Leu Glu Pro Phe Arg Met	1e Arg Met
	210 215	5 220		405 410	415
	Asp Leu Lys Thr Tyr Phe Thr Asp Lys Lys Thr Hi	r Asp Lys Lys Thr His 3	s Leu Tyr Thr Leu	Thr Pro Phe Ser Ala Ile Gly Leu Glu Leu Trp Ser Met Thr Ser Asp	r Ser Asp
70	225 . 230	235	240	.20 . 420 . 425 4.	430
	ile Leu Asn Pro Asp Asn Ser Phe Glu Ile Leu Val Asp Gln Ser Val	r Phe Glu Ile Leu Val 1	Asp Gln Ser Val	Ile Phe Phe Asp Asn Phe Ile Ile Cys Ala Asp Arg Arg Ile Val	e Val Asp
	245	250	255	435 440 445	
	Val Asn Ser Gly Asn Leu Leu Asn Asp Met Thr Pro Pro Val Asn Pro	J Asn Asp Met Thr Pro 1	Pro Val Asn Pro	Asp Trp Ala Asn Asp Gly Trp Gly Leu Lys Lys Ala Ala Asp Gly	p Gly Ala
	260	265	270	450 455 460	

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PCT/EP2003/014057		ac 2002: Q07021			Pro Arg Val Leu Gly Ser Ser Ve	10 15	Ala Ser Pro Phe Arg Gln Leu Le	25 30	Arg Pro Phe Gly Leu Leu Ser Ve	45	Gly Leu Leu Arg Pro Arg Gly Pr	09	Ser Leu His Thr Asp Gly Asp Ly	75 80	Glu Ile Lys Glu Glu Arg Lys Il	90 95	Met Ser Gly Gly Trp Glu Leu Gl	105 110	Val Arg Lys Val Ala Gly Glu Ly	. 125	Asn Ser Ile Pro Pro Thr Phe As	140	Gln Lys Val Glu Glu Gln Glu Pr	155	
WO 2004/055519	<222> (1)(282)	<223> Accession No. as of 09 Dec 2002: Q07021	<400> 41		5 Met Leu Pro Leu Leu Arg Cys Val Pro Arg Val Leu Gly Ser Ser Val	· T	Ala Gly Leu Arg Ala Ala Aro Ala Ser Pro Phe Arg Gln Leu Leu	20	Gln Pro Ala Pro Arg Leu Cys Thr Arg Pro Phe Gly Leu Leu Ser Val	10 35 40	Arg Ala Gly Ser Glu Arg Arg Pro Gly Leu Leu Arg Pro Arg Gly Pro	50 55	Cys Ala Cys Gly Cys Gly Cys Gly Ser Leu His Thr Asp Gly Asp Lys	65 70	15 Ala Phe Val Asp Phe Leu Ser Asp Glu Ile Lys Glu Glu Arg Lys Ile		Gln Lys His Lys Thr Leu Pro Lys Met Ser Gly Gly Trp Glu Leu Glu	100	Leu Asn Gly Thr Glu Ala Lys Leu Val Arg Lys Val Ala Gly Glu Lys	20 115 . 120	ile Thr Val Thr Phe Asn ile Asn Asn Ser Ile Pro Pro Thr Phe Asp	130 135	Gly Glu Glu Bro Ser Gln Gly Gln Lys Val Glu Glu Gln Glu Fro	145 150	
14057																									
PCT/EP2003/014057	a Glu Glu Arg	480	u Pro Val Phe	495	ır Ser Gly Met	510	s Glu Glu Glu	ξ.	u Glu Glu Gly		u Glu Asp Gly	260	s Ala Glu Glu	575	o Arg Arg Glu	290				·					
	Ala Glu Pro Gly Val Val Gly Gln Met Ile Glu Ala Ala Glu Glu Arg	475	Pro Trp Leu Trp Val Val Tyr Ile Leu Thr Val Ala Leu Pro Val Phe	490	Leu Val Ile Leu Phe Cys Cys Ser Gly Lys Lys Gln Thr Ser Gly Met		Glu Tyr Lys Lys Thr Asp Ala Pro Gln Pro Asp Val Lys Glu Glu Glu	525	Glu Glu Lys Glu Glu Lys Asp Lys Gly Asp Glu Glu Glu Glu Gly	540	Glu Glu Lys Leu Glu Glu Lys Gln Lys Ser Asp Ala Glu Glu Asp Gly	555	Gly Thr Val Ser Gln Glu Glu Glu Asp Arg Lys Pro Lys Ala Glu Glu	570	Asp Glu Ile Leu Asn Arg Ser Pro Arg Asn Arg Lys Pro Arg Arg Glu										•
129/335	al Gly Gln Met	470	al Tyr Ile Leu		rs Cys Ser Gly	505	sp Ala Pro Gln	520	lu Lys Asp Lys	535	lu Lys Gln Lys	550	lu Glu Glu Asp		rg Ser Pro Arg	585								ponent 1	
	Pro Gly Val V	4	Leu Trp Val V	485	Ile Leu Phe C	200	Lys Lys Thr A	515	Lys Glu Glu G		Lys Leu Glu G	ĬĠ	Val Ser Gln G	565	Ile Leu Asn A	580		•	41	282	PRT	Homo sapiens		<221> Complement component	
WO 2004/055519	Ala Glu	465	Pro Trp		5 Leu Val		. Glu Tyr		Glu Glu	10 530	Glu Glu	545	Gly Thr		15 Asp Glu				<210> 4	20 <211> 2	<212> F	<213> F	<220>	<221> (

WO 20	WO 2004/055519	131/335	PCT/EP2003/014057		WO 2004/055519	132/335	8	PCT/EP2003/014057
Glu	Glu Leu Thr Ser Thr Pro Asn Phe Val Val Glu Val Ile		Lys Asn Asp		precursor	rsor		
٠	165	170	175		<222> (1)(727)	(727)		
Asp	Asp Gly Lys Lys Ala Leu Val Leu Asp Cys His Tyr Pro		Glu Asp Glu		<223> Acces	Accession No. as of 09 Dec 2002: P28331	2002: P28331	
	180	185	. 061		<400> 42		•	
5 Val	Val Gly Gln Glu Asp Glu Ala Glu Ser Asp Ile Phe Ser		Ile Arg Glu		vo			
	195 200	205			Met Leu Arg	Met Leu Arg Ile Pro Val Arg Arg Ala Leu Val Gly Leu Ser Lys Ser	a Leu Val Gly Leu Se	er Lye Ser
Val	Val Ser Phe Gin Ser Thr Gly Glu Ser Glu Trp Lys Asp		Thr Asn Tyr			·	10	15
	210 215	220		4	. Pro Lys Gly (Pro Lys Gly Cys Val Arg Thr Thr Ala Thr Ala Ala Ser Asn Leu Ile	Thr Ala Ala Ser As	an Leu Ile
Thr	Thr Leu Asn Thr Asp Ser Leu Asp Trp Ala Leu Tyr Asp		His Leu Met		,	20 25	30	
10 225	230	235	240		10 Glu Val Phe V	Glu Val Phe Val Asp Gly Gln Ser Val Met Val Glu Pro Gly Thr Thr	. Met Val Glu Pro Gl	ly Thr Thr
Asp	Asp Phe Leu Ala Asp Arg Gly Val Asp Asn Thr Phe Ala		Asp Glu Leu		35	40	45	
	245	250	255		Val Leu Gln A	Val Leu Gln Ala Cys Glu Lys Val Gly Met Gln Ile Pro Arg Phe Cys	' Met Gln Ile Pro Ar	g Phe Cys
Val	Val Glu Leu Ser Thr Ala Leu Glu Hia Gln Glu Tyr Ile	u His Gln Glu Tyr Ile T	Thr Phe Leu		. 20	. co	09	
	260	265	270		Tyr His Glu A	Tyr His Glu Arg Leu Ser Val Ala Gly Asn Cys Arg Met Cys Leu Val	Asn Cys Arg Met Cy	rs Leu Val
15 Glu 2	Glu Asp Leu Lys Ser Phe Val Lys Ser Gln	s Ser Gln			15 65	. 04	75	. 08
	275 280	0			Glu Ile Glu L	Glu Ile Glu Lys Ala Pro Lys Val Val Ala Ala Cys Ala Met Pro Val	Ala Ala Cys Ala Me	it Pro Val
						85	06	
					Met Lys Gly T	Met Lys Gly Trp Asn Ile Leu Thr Asn Ser Glu Lys Ser Lys Lys Ala	Ser Glu Lys Ser Ly	s Lys Ala
<210>	42				н	100 105	110	0
20 <211>	727				20 Arg Glu Gly V	Arg Glu Gly Val Met Glu Phe Leu Leu Ala Asn His Pro Leu Asp Cys	Ala Asn His Pro Le	и Авр Сув
<212>	• PRT				115	. 120	125	
<213>	• Homo sapiens				Pro Ile Cys A	Pro Ile Cys Asp Gln Gly Gly Glu Cys Asp Leu Gln Asp Gln Ser Met	Asp Leu Gln Asp Glr	n Ser Met
<220>					130	135	140	
<221>	<221> NADH-ubiquinone oxidoreductase 75 KDa subunit.	inctase 75 kDa subunit,	mitochondrial		Met Phe Gly A	Met Phe Gly Asn Asp Arg Ser Arg Phe Leu Glu Gly Lys Arg Ala Val	Leu Glu Gly Lys Arg	g Ala Val

WO 2004/055519 PCT/EP2003/014057	340 345 350	Ata Leu Lys Asp Leu Leu Asn Arg Val Asp Ser Asp Thr Leu Cys Thr 355 360 365	Glu Glu Val Phe Pro Thr Ala Gly Ala Gly Thr Asp Leu Arg Ser Asn	5 370 375 380 Tyr Leu Leu Aen Thr Thr Ile Ala Gly Val Glu Glu Ala Aep Val Val	385 390 395 400	Leu Leu Val Gly Thr Asn Pro Arg Phe Glu Ala Pro Leu Phe Asn Ala	10 Trp Ile Arg Lys Ser Trp Leu His Asn Asp Leu Lys Val Ala Leu Ile 420 425 430	Gly Ser Pro Val Asp Leu Thr Tyr Thr Tyr Asp His Leu Gly Asp Ser	435 440 445	Pro Lys Ile Leu Gln Asp Ile Ala Ser Gly Ser	460 Val Leu Lys Glu Ala Lys Lys Pro Met Val Val Leu Gly Ser Ser Ala	465 470 475 480	reu din Arg Asn Asp Gly Ala Ala Ile Leu Ala Ala Val Ser Ser Ile	485 490 . 495	20 Ala Gln Lys Ile Arg Met Thr Ser Gly Val Thr Gly Asp Trp Lys Val	500 505 510	Met Asn Ile Leu His Arg Ile Ala Ser Gin Val Ala Ala Leu Asp Leu	515 520 525	Gly Tyr Lys Pro Gly Val Glu Ala Ile Arg Lys Asn Pro Pro Lys Val	
WO 2004/055519 PCT/EP2003/014057	145 150 155. 160	ord may mys man its oly mro med val Lys int ile Met Thr Arg Cys 165	ile Gln Cys Thr Arg Cys ile Arg Phe Ala Ser Glu ile Ala Gly Val	180 189 Asp Leu Gly Thr Thr Gly Arg Gly Asn Asp Met Gln Val Gly Thr	195 200 205	Tyr ile Glu Lys Met Phe Met Ser Glu Leu Ser Gly Asn ile ile Asp	10 Ile Cys Pro Val Gly Ala Leu Thr Ser Lys Pro Tyr Ala Phe Thr Ala 225 230 235 240	Arg Pro Trp Glu Thr Arg Lys Thr Glu Ser Ile Asp Val Met Asp Ala	245 250 255	Thr Arg Thr Gly Glu	Z/O Met His Glu Asp Ile Asn Glu Glu Trp Ile S	275 280 285	Lys Thr Arg Phe Ala Tyr Asp Gly Leu Lys Arg Gln Arg Leu Thr Glu	290· 295 300	Pro Met Val Arg Asn Glu Lys Gly Leu Leu Thr Tyr Thr Ser Trp Glu	305 310 315 320	Asp Ala Leu Ser Arg Val Ala Gly Met Leu Gln Ser Phe Gln Gly Lys	325 330 335 .	Asp Val Ala Ala Ile Ala Gly Gly Leu Val Asp Ala Glu Ala Leu Val	

	WO 2004/055519	135/335	PCT/EP2003/014057		WO 2004/055519	136/33\$	PCT/EP2003/0
	530 535	5 540	0			725	
	Leu Phe Leu Leu Gly Ala Asp Gly Gly Cys Ile Thr Arg Gln Asp Leu	oly Gly Cys Ile Th	r Arg Gln Asp Leu				
	545 550	555	260		-		•
	Pro Lys Asp Cys Phe Ile Ile Tyr Gln Gly His His Gly Asp Val Gly	Tyr Gln Gly His His	s Gly Asp Val Gly		<210> 43		
	5 565	570	575	-	5 <211> 491		
	Ala Pro Ile Ala Asp Val Ile Leu Pro Gly Ala Ala Tyr Thr Glu Lys	teu Pro Gly Ala Ale	a Tyr Thr Glu Lys		<212> PRT		
	280	585	590		<213> Homo sapiens	piens	·
	Ser Ala Thr Tyr Val Asn Thr Glu Gly Arg Ala Gln Gln Thr Lys Val	. Glu Gly Arg Ala Gln	ı Gln Thr Lys Val		<220>		
	595	009	605		<221> Pre-B C	Pre-B cell enhancing factor precursor	scursor
10	Ala Val Thr Pro Pro	Ala Arg Glu Asp Trp) Lys Ile Ile Arg	10	(1)(491)	11)	
	610 615	620			<223> Accession No.	on No. as of 09 Dec 2002; P43490): P43490
	Ala Leu Ser Glu Ile Ala Gly Met Thr Leu Pro Tyr Asp Thr Leu Asp	Met Thr Leu Pro Tyr	. Asp Thr Leu Asp		<400> 43	£	
	625 630	635	640				
	Gln Val. Arg Asn Arg Leu Glu Glu Phe Ser Pro Asn Leu Val Arg Tyr	Glu Phe Ser Pro Asn	Leu Val Arg Tyr		Met Asn Pro Ale	Ala Glu Ala Glu Phe Ası	Met Asn Pro Ala Ala Glu Ala Glu Phe Asn Ile Leu Leu Ala Thr Asp
15	645	650	655	15			15
	Asp Asp ile Glu Gly Ala Asn Tyr Phe Gln Gln Ala Asn Glu Leu Ser	Tyr Phe Gln Gln Ala	Asn Glu Leu Ser		Ser Tyr Lys Val	. Thr His Tyr Lys Gln Ty	Ser Tyr Lys Val Thr His Tyr Lys Gln Tyr Pro Pro Asn Thr Ser Lys
	099		670		20	. 52	30
	Lys Leu Val Asn Gin Gin Leu Leu Ala Asp Pro Leu Val Pro Pro Gin	Leu'Ala Asp Pro Leu	Val Pro Pro Gln		Val Tyr Ser Tyr	Phe Glu Cys Arg Glu Lys	Val Tyr Ser Tyr Phe Glu Cys Arg Glu Lys Lys Thr Glu Asn Ser Lys
	. 675	680	685		35	40	45
20	Leu Thr Leu Lys Asp Phe Tyr Met Thr Asp Ser Il	Met Thr Asp Ser Ile	e Ser Arg Ala Ser	20		Lys Tyr Glu Glu Thr Val	beu Arg Lys Val Lys Tyr Glu Glu Thr Val Phe Tyr Gly Leu Gln Tyr
	699	700			. 20	. 55	
	Gin Thr Met Ala Lys Cys Val Lys Ala Val Thr Glu Gly Ala Gin Ala	Lys Ala Val Thr Glu	Gly Ala Gln Ala		Ile Leu Asn Lys	Tyr Leu Lys Gly Lys Val	Ile Leu Asn Lys Tyr Leu Lys Gly Lys Val Val Thr Lys Glu Lys Ile
	705 710	715.	720		. 9	7.0	75 80
	Val Glu Glu Pro Ser Ile Cys				Gln Glu Ala Lys	Asp Val Tyr Lys Glu His	Gin Giu Ala Lys Asp Val Tyr Lys Giu His Phe Gin Asp Asp Val Phe

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	WO 2004/055519	137/335	PCT/EP2003/014057	WO 2004/055519	PC 138/335	PCT/EP2003/01
	89 S2	06		275	280 285	
	Asn Glu Lys Gly Trp Asn Tyr Ile Leu Glu Lys Tyr Asp Gly His Leu	Ile Leu Glu Lys Tyr Asp G	Aly His Leu	Lys Ile Trp Gly Glu Asp Le	Lys lle Trp Gly Glu Asp Leu Arg His Leu lle Val Ser Arg Ser Thr	Ser Thr
	100	105	110	290 295	300	
	Pro Ile Glu Ile Lys Ala Val Pro Glu Gly Phe Val Ile Pro Arg Gly	Pro Glu Gly Phe Val Ile P	ro Arg Gly		Gin Ala Pro Leu ile ile Arg Pro Asp Ser Gly Asn Pro Leu Asp Thr	Asp Thr
	5 115	120 125			315	320
	Asn Val Leu Phe Thr Val Glu Asn Thr Asp Pro Glu Cys Tyr	Asn Thr Asp Pro Glu Cys T	yr Trp Leu	Val Leu Lys Val Leu Glu Il	Val Leu Lys Val Leu Glu Ile Leu Gly Lys Lys Phe Pro Val Thr Glu	Thr Glu
	130 135	140		325	330	335
	Thr Asn Try Ile Glu Thr Ile Leu Val Gln Ser Try fyr Pro Ile Thr	beu Val Gln Ser Trp Tyr P	ro lle Thr	Asn Ser Lys Gly Tyr Lys Les	Asn Ser Lys Gly Tyr Lys Leu Leu Pro Pro Tyr Leu Arg Val Ile Gln	tle Gln
	145	155	160	. 340	345 . 350	
10	Val Ala Thr	Gin Lys Lys lie Leu Ala L $_{ m D}$	ys Tyr Leu 10		Gly Asp Gly Val Asp Ile Asn Thr Leu Gln Glu Ile Val Glu Gly Met	Jy Met
-	. 165	170	175	355	360 365	
	Leu Glu Thr Ser Gly Asn Leu Asp Gly Leu Glu Ty	Asp Gly Leu Glu Tyr Lys Le	r Lys Leu His Asp	Lys Gln Lys Met Trp Ser Ile	Lys Gln Lys Met Trp Ser Ile Glu Asn Ile Ala Phe Gly Ser Gly Gly	11y Gly
	180	185 190	00	376 375	380	
	Phe Gly Tyr Arg Gly Val Ser Ser Gln Glu Thr Ala	Ser Gln Glu Thr Ala Gly Il	Gly ile Gly Ala	Gly beu beu Gln bys beu Thr	Gly Leu Leu Gin Lys Leu Thr Arg Asp Leu Leu Asn Cys Ser Phe Lys	he Lys
15	195	200 205	S1	385 390	395	400
	Ser Ala His Leu Val Asn Phe Lys Gly Thr Asp Thr Val Ala Gly Leu	ys Gly Thr Asp Thr Val Al	а СЈУ Љец	Cys Ser Tyr Val Val Thr Asn	Cys Ser Tyr Val Val Thr Asn Gly Leu Gly Ile Asn Val Phe Lys Asp	ув Авр
	210 215	220		405	410	415
	Ala Leu Ile Lys Lys Tyr Tyr Gly Thr Lys Asp Pro		Val Pro Gly Tyr	Pro Val Ala Asp Pro Asn Lys	Pro Val Ala Asp Pro Asn Lys Arg Ser Lys Lys Gly Arg Leu Ser Leu	er Leu
	225 230	235	240	420	425 430	
20	Ser Val Pro Ala Ala Glu His Ser Thr Ile Thr Ala		Trp Gly Lys Asp 20	His Arg Thr Pro Ala Gly Asn	His Arg Thr Pro Ala Gly Asn Phe Val Thr Leu Glu Glu Gly Lys Gly	ув Gly
	245	250	255	435	440	
	His Glu Lys Asp Ala Phe Glu His Ile Val Thr Gln		Phe Ser Val	Asp Leu Glu Glu Tyr Gly Gln	Asp Leu Glu Glu Tyr Gly Gln Asp Leu Leu His Thr Val Phe Lys Asn	/8 Asn
	260	265 270	6	450 455	460	
	Pro Val Ser Val Val Ser Asp Ser Tyr Asp Ile Tyr		Asn Ala Cys Glu	Gly Lys Val Thr Lys Ser Tyr	Gly Lys Val Thr Lys Ser Tyr Ser Phe Asp Glu 11e Arg Lys Asn Ala	n Ala

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PCT/EE	80 75 80 Arg Lys Cys Met Thr Thr Val Ser Trp Asp Gly Asp Lys Leu Gln Cys	Val Gln Lvs Glv Glu Lvs Glu	100 105 110 110 110 110 110 110 110	Leu His Leu Glu Met Arg Val Glu Gly	115 120 125 Gln Val Phe Lys Lys Val Gln	130 135			<210> 45	<211> 544	<212> PRT	15 <213> Homo sapiens	<220>	<221> T-complex protein 1, gamma subunit	<222> (1)(544) "	<223> Accession No. as of 09 Dec 2002: P49368	20 <400> 45	Met Gly His Arg Pro Val Leu Val Leu Ser Gln Asn Thr Lys Arg Glu	1 5 10 15	Ser Gly Arg Lys Val Gln Ser Gly Asn Ile Asn Ala Ala Lys Thr Ile		
PCT/EP2003/014057	480												ı Val Asn Glu Asn	15	Ala Leu Arg Lys	. 08	Gln Asp Gly Asp 45	Tyr ile Met Asp		Gly lle Asp Asp		
WO 2004/055519 139/335	Leu Asn Ile Glu Leu Glu Ala Ala His	485 490		<210> 44		<213> Homo sapiens	<2220>	<221> Retinol-binding protein I, cellular	<222> (1)(135)	<223> Accession No. as of 09 Dec 2002: P09455	<400> 44		Met Pro Val Asp Phe Thr Gly Tyr Trp Lys Met Leu Val Asn Glu As	5 10	Phe Glu Glu Tyr Leu Arg Ala Leu Asp Val Asn Val Ala Leu Arg Ly!	20 25	Ile Ala Asn Leu Leu Lys Pro Asp Lys Glu Ile Val Gln Asp Gly Asp 35	His Met Ile Ile Arg Thr Leu Ser Thr Phe Arg Asn Tyr Ile Met Asp	50 55 60	Phe Gln Val Gly Lys Glu Phe Glu Glu Asp Leu Thr Gly Ile Asp Asp		

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WO 2004/055519	PCT/EP2003/014057	WO 2004/055519 PCT/EP2003/014057
20	25 30	210 215 220
Ala Asp Ile Ile Arg Thr Cys 1	Ala Asp Ile Ile Arg Thr Cys Leu Gly Pro Lys Ser Met Met Lys Wet	His Pro Arg Met Arg Tyr Ile Lys Asn Pro Arg Ile Val Leu Leu
35	40 45	. 225 230 235 240
Leu Leu Asp Pro Met Gly Gly 1	Leu Leu Asp Pro Met Gly Gly Ile Val Met Thr Asn Asp Gly Asn Ala	Asp Ser Ser Leu Glu Tyr Lys Lys Gly Glu Ser Gln Thr Asp Ile Glu
5 50 55	09	5 245 250 255
Ile Leu Arg Glu Ile Gln Val G	Ile Leu Arg Glu Ile Gln Val Gln His Pro Ala Ala Lys Ser Met Ile	lle Thr Arg Glu Glu Asp Phe Thr Arg Ile Leu Gln Met Glu Glu Glu
0.2	75 80	260 265 270
Glu Ile Ser Arg Thr Gln Asp G	Glu Ile Ser Arg Thr Gln Asp Glu Glu Val Gly Asp Gly Thr Thr Ser	Tyr lle Gln Gln Leu Cys Glu Asp lle 11e Gln Leu Lys Pro Asp Val
. 85	. 56 06	275 280 285
10 Val Ile Ile Leu Ala Gly Glu Met Leu Ser Val Ala Gl	fet Leu Ser Val Ala Glu His Phe Leu	10 Val Ile Thr Glu Lys Gly Ile Ser Asp Leu Ala Gln His Tyr Leu Met
100	105	290 295 300
Glu Gln Gln Met His Pro Thr V	Glu Gln Gln Met His Pro Thr Val Val Ile Ser Ala Tyr Arg Lys Ala	Arg Ala Asn 11e Thr Ala 11e Arg Arg Val Arg Lys Thr Asp Asn Asn
115 12	120	305 310 315 320
Leu Asp Asp Met Ile Ser Thr L	Leu Asp Asp Met Ile Ser Thr Leu Lys Lys Ile Ser Ile Pro Val Asp	Arg Ile Ala Arg Ala Cys Gly Ala Arg Ile Val Ser Arg Pro Glu Glu
15 130 135	140	15 325 330 335
Ile Ser Asp Ser Asp Met Met L	ile Ser Asp Ser Asp Met Met Leu Asn Ile Ile Asn Ser Ser Ile Thr	Leu Arg Glu Asp Asp Val Gly Thr Gly Ala Gly Leu Leu Glu Ile Lys
145	. 155	340 345 350
Thr Lys Ala Ile Ser Arg Trp Ser Ser Leu Ala Cys Asn	er Ser Leu Ala Cys Asn Ile Ala Leu	Lys ile Gly Asp Glu Tyr Phe Thr Phe Ile Thr Asp Cys Lys Asp Pro
165	. 176 175	355 360 365
20 Asp Ala Val Lys Met Val Gln Phe Glu Glu Asn Gly Arg	he Glu Glu Asn Gly Arg Lys Glu Ile	20 Lys Ala Cys Thr Ile Leu Leu Arg Gly Ala Ser Lys Glu Ile Leu Ser
180	185 190	370 375 380
Asp ile Lys Lys Tyr Ala Arg Va	Asp lie Lys Lys Tyr Ala Arg Val Glu Lys lie Pro Gly Gly lie lie	Glu Val Glu Arg Asn Leu Gln Asp Ala Met Gln Val Cys Arg Asn Val
195	200 205	395 390 395 400
Glu Asp Ser Cys Val Leu Arg Gly Val Met Ile Asn Ly	ly Val Met Ile Asn Lys Asp Val Thr	Leu Leu Asp Pro Gln Leu Val Pro Gly Gly Gly Ala Ser Glu Met Ala

	WO 2004/055519 PCT/EP2003/014057	WO 2004/055519 PCT/EP2003/014057 144/335
	405 410 415	<221> Placental ribonuclease inhibitor
	Val Ala His Ala Leu Thr Glu Lys Ser Lys Ala Met Thr Gly Val Glu	<222> (1)(461)
•	420 425 430 .	<223> Accession No. as of 09 Dec 2002: 213489
	Gin Trp Pro Tyr Arg Ala Val Ala Gin Ala Leu Giu Val Ile Pro Arg ,	<400> 46
.0.	435 440 445	19
	Thr Leu Ile Gln Asn Cys Gly Ala Ser Thr Ile Arg Leu Leu Thr Ser	Met Ser Leu Asp Ile Gln Ser Leu Asp Ile Gln Cys Glu Glu Leu Ser
	450 . 455 . 460	1 5 10 15
	Leu Arg Ala Lys Hie Thr Gln Glu Asn Cys Glu Thr Trp Gly Val Asn	Asp Ala Arg Trp Ala Glu Leu Leu Pro Leu Leu Gln Gln Cys Gln Val
	465 470 475 480	20 25 30
10	Gly Glu Thr Gly Thr Leu Val Asp Met Lys Glu Leu Gly Ile Trp Glu	Val Arg Leu Asp Asp Cys Gly Leu Thr Glu Ala Arg Cys Lys Asp Ile
	485 490 495	35 40 45
	Pro Leu Ala Vel Lys Leu Gln Thr Tyr Lys Thr Ala Vel Glu Thr Ala	Ser Ser Ala Leu Arg Val Asn Pro Ala Leu Ala Glu Leu Asn Leu Arg
	500 505 510	55 60
	Val Leu Leu Arg Ile Asp Asp Ile Val Ser Gly His Lys Lys Lys	Ser Asn Glu Leu Gly Asp Val Gly Val His Cys Val Leu Gln Gly Leu
15	515 520 525 15	65 70 75 80
	Gly Asp Asp Gln Ser Arg Gln Gly Ala Pro Asp Ala Gly Gln Glu	Gln Thr Pro Ser Cys Lys 1le Gln Lys Leu Ser Leu Gln Asn Cys Cys
	530 535 540	S6 06 S8
		Leu Thr Gly Ala Gly Cys Gly Val Leu Ser Ser Thr Leu Arg Thr Leu
		100 105 110
70	<210> 46 20	Pro Thr Leu Gln Glu Leu His Leu Ser Asp Asn Leu Leu Gly Asp Ala
	<211> 461	115 120 .125
	<212> PRT	Gly Leu Gln Leu Leu Cys Glu Gly Leu Leu Asp Pro Gln Cys Arg Leu
	<213> Homo sapiens	130 135 140
	<220>	Glu Lys Leu Gln Leu Glu Tyr Cys Ser Leu Ser Ala Ala Ser Cys Glu

3/014057 WO 2004/05S519 PCT/EP2003/014057	340 345 350	Leu Glu Asp Ala Gly Val Arg Glu Leu Cys Gln Gly Leu Gly Gln Pro	355 360 365	Gly Ser Val Leu Arg Val Leu 1rp Leu Ala Asp Cys Asp Val Ser Asp	5 370 375 380	Ser Ser Ser Ser Leu Ala Ala Thr Leu Leu Ala Asn His Ser Leu	385 390 395	Arg Glu Leu Asp Leu Ser Asn Asn Cys Leu Gly Asp Ala Gly Ile Leu	405 410 . 415	10 Gln Leu Val Glu Ser Val Arg Gln Pro Gly Cys Leu Leu Glu Gln Leu	420 425 430	Val Leu Tyr Asp Ile Tyr Trp Ser Glu Glu Met Glu Asp Arg Leu Gln	435 440 445	Ala Leu Glu Lys Asp Lys Pro Ser Leu Arg Val Ile Ser	15 450 455 460			<210> 47	<211> 317	20 <212> PRT	<213> Homo sapiens		1044
993	160	Glu Leu Thr	175	Leu Cys Gln	190	s Leu Glu Ser	ις.	y ile Val Ala		sn Lys Leu Gly	240	is Pro Ser Ser	255	Ala Lys Gly	270	eu Lys Glu		Arg Leu Leu		er Leu Trp Val	320	he Ser Ser Val	
PCT/EP2003/014057	so.			l Arg Val	-	a Leu Ly	. 205	u Cys G	220	Y Ser A	ıs	u Leu H		7 Ile Thr		s Glu Ser I	285	Gly Ala	300	Glu S	,-	a	}
PCT/EP2	155	Pro Leu Ala Ser Val Leu Arg Ala Lys Pro Asp Phe Lys	170	Val Ser Asn Asp Ile Asn Glu Ala Gly Val Arg Val	185	Gly Leu Lys Asp Ser Pro Cys Gln Leu Glu Ala Leu Lys Leu Glu Ser	200 . 20	Cys Gly Val Thr Ser Amp Amn Cys Arg Amp Leu Cym Gly Ile Val Ala	215 220	Ser Lys Ala Ser Leu Arg Glu Leu Ala Leu Gly Ser Asn Lys Leu Gly	235	Asp Val Gly Met Ala Glu Leu Cys Pro Gly Leu Leu His	250	Arg Leu Arg Thr Leu Trp Ile Trp Glu Cys Gly Ile Thr Ala Lys Gly	265	Cys Gly Asp Leu Cys Arg Val Leu Arg Ala Lys Glu Ser Leu Lys Glu	280 285	Leu Ser Leu Ala Gly Asn Glu Leu Gly Asp Glu Gly Ala Arg Leu Leu	300	Cys Glu Thr Leu Leu Glu Pro Gly Cys Gln Leu Glu Ser Leu Trp Val	315	Lys Ser Cys Ser Phe Thr Ala Ala Cys Cys Ser His Phe S	

Asp Lys Leu Val Asn His Ile Gly Asp Gly Ser Leu 205 Trp Asp Leu Asn 220 Ile Ile Asn Ala 235 Ala Thr Gly Pro
165 10 Asn Cys Lys Leu Lys Thr Asn His Ile Gly His Thr 10 185 190 180 185 190 200 205 ys Asp Gly Gln Ala Met Leu Trp Asp Leu Asn Glu Gly 215 220 yr Thr Leu Asp Gly Gly Asp Ile Ile Asn Ala Leu Cys 230 230 235 240 sn Arg Tyr Trp Leu Cys Ala Ala Thr Gly Pro Ser Ile
la Asn Cys Lys Leu Lys Thr Asn His Ile Gly His Thr 80 185 190 200 205 ys Asp Gly Gln Ala Met Leu Trp Asp Leu Asn Glu Gly 215 215 220 yr Thr Leu Asp Gly Gly Asp Ile Ile Asn Ala Leu Cys 81 Arg Tyr Trp Leu Cys Ala Ala Ala Thr Gly Pro Ser Ile
80
Thr Val Thr Val Ser Pro Asp Gly Ser Leu Cys Ala 200 205 #### 200 205 #### 200 205 #### 200 205 #### 200 205 #### 200 205 #### 200 200 #### 200 200 #### 200 200 #### 200 200 #### 200 200 #### 200 200 #### 200 200 #### 200 200 #### 200 200 #### 200 200 #### 200 200 #### 200 200 #### 200 200 ##### 200 200 ##### 200 200 ##### 200 200 ##### 200 200 ##### 200 200
200 205 ys Asp Gly Gln Ala Met Leu Trp Asp Leu Asn Glu Gly 215 220 yr Thr Leu Asp Gly Gly Asp Ile Ile Asn Ala Leu Cys 230 230 235 240 sn Arg Tyr Trp Leu Cys Ala Ala Thr Gly Pro Ser Ile
ys Asp Gly Gln Ala Met Leu Trp Asp Leu Asn Glu Gly 215 220 yr Thr Leu Asp Gly Gly Asp Ile Ile Asn Ala Leu Cys 230 235 240 sn Arg Tyr Trp Leu Cys Ala Ala Thr Gly Pro Ser Ile
215 220 yr Thr Leu Asp Gly Gly Asp Ile Ile Asn Ala Leu Cys 230 235 240 sn Arg Tyr Trp Leu Cys Ala Ala Thr Gly Pro Ser Ile
yr Thr Leu Asp Gly Gly Asp Ile Ile Asn Ala Leu Cys 230 210 215 Sn Arg Tyr Trp Leu Cys Ala Ala Thr Gly Pro Ser Ile
230 240 sn Arg Tyr Trp Leu Cys Ala Ala Thr Gly Pro Ser Ile
sn Arg Tyr Trp Leu Cys Ala Ala Thr Gly Pro Ser Ile
250 255
Lys ile Trp Asp Leu Glu Gly Lys ile ile Val Asp Glu Leu Lys Gln
260 . 265 . 270
Glu Val Ile Ser Thr Ser Ser Lys Ala Glu Pro Pro Gln Cys Thr Ser
280 . 285
Leu Ala Trp Ser Ala Asp Gly Gln Thr Leu Phe Ala Gly Tyr Thr Asp
295 300
Asn Leu Val Arg Val Trp Gln Val Thr Ile Gly Thr Arg
310 315
ar Ala er Thr

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WO 2004/055519 PCT/EP2003/014057	Thr Met Gly Asp Arg Phe Thr Asp Glu Glu Val Asp Glu Met Tyr Arg	. 130 135 140	Glu Ala Pro Ile Asp Lys Lys Gly Asn Phe Asn Tyr Val Glu Phe Thr	145 150 155 160	5 Arg Ile Leu Lys His Gly Ala Lys Asp Asp	165 170		<210> 49	10 <211> 114	<212> PRT	<213> Homo sapiens	<220>	<221> Calgranulin B	15 <222> (1)(114)	<223> Accession No. as of 10 Dec 2002: P06702	<400> 49 · · ·		Met Thr Cys Lys Met Ser Gln Leu Glu Arg Asn Ile Glu Thr Ile Ile	20 1 5 10 15	Asn Thr Phe His Gln Tyr Ser Val Lys Leu Gly His Pro Asp Thr Leu	20 25 30	Asn Gln Gly Glu Phe Lys Glu Leu Val Arg Lys Asp Leu Gln Asn Phe	35 40 45	
WO 2004/055519 PCT/EP2003/014057 149/335	<212> PRT	<213> Homo sapiens	<220>	<221> Myosin regulatory light chain 2	<222> (1)(172)	<223> Accession No. as of 10 Dec 2002; P24844	<400>	Met Ser Eys Arg Ala Lys Ala Lys Thr Thr Lys Lys Arg Pro Gln	10 1 5 10 15	Arg Ala Thr Ser Asn Val Phe Ala Met Phe Asp Gin Ser Gin Ile Gin	20 25 30	Glu Phe Lys Glu Ala Phe Asn Met Ile Asp Gln Asn Arg Asp Gly Phe	35 40 45	15 Ile Asp Lys Glu Asp Leu His Asp Met Leu Ala Ser Leu Gly Lys Asn	50 55 60	Pro Thr Asp Glu Tyr Leu Glu Gly Met Met Ser Glu Ala Pro Gly Pro	65 70 75 80	Ile Asn Phe Thr Met Phe Leu Thr Met Phe Gly Glu Lys Leu Asn Gly		Thr Asp Pro Glu Asp Val Ile Arg Asn Ala Phe Ala Cys Phe Asp Glu	100 105 110	Glu Ala Ser Gly Phe Ile His Glu Asp His Leu Arg Glu Leu Leu Thr	115 120 125	

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		151/335				152/335	
Leu Lys Ly	Leu Lys Lys Glu Asn Lys Asn Glu Lys Val Ile Glu Hi	Glu Lys Val Ile	Glu His Ile Met Glu		Gln Asp Pro Gly Leu His Val Trp Arg Val Glu Lys Leu Lys Pro Val	rp Arg Val Glu Lys	Leu Lys Pro Val
20	55		90		20		30
Asp Leu As	Asp Leu Asp Thr Asn Ala Asp Lys Gln Leu Ser Phe Gl	Lys Gln Leu Ser	Phe Glu Glu Phe Ile		Pro Val Ala Glu Aen Glu Gly Vel Phe Phe Ser Gly Asp Ser Tyr	ly Val Phe Phe Ser	Gly Asp Ser Tyr
65	70	75	80		35	40	45
5 Met Leu Me	et Ala Arg Leu Thr	Trp Ala Ser His	Met Leu Met Ala Arg Leu Thr Trp Ala Ser His Glu Lys Met His Glu	In	Leu Val Leu His Asn Gly Pro Glu Glu Val Ser His Leu His Leu Trp	du Glu Val Ser His	Leu His Leu Trp
	82	06	95		50 55	09	
Gly Asp Gl	Gly Asp Glu Gly Pro Gly His His His Lys Pro Gly Leu	His His Lys Pro	Gly Leu Gly Glu Gly		Ile Gly Gln Gln Ser Arg Asp Glu Gln Gly Ala Cys Ala Val Leu	sp Glu Gln Gly Ala	Cys Ala Val Leu
	100	105	110		. 20 20	75	08
Thr Pro				,	Ala Val His Leu Asn Thr Leu Leu Gly Glu Arg Pro Val Gln His Arg	eu Gly Glu Arg Pro	Val Gln His Arg
10				01	85	06	95
÷					Glu Val Gln Gly Asn Glu Ser Asp Leu Phe Met Ser Tyr Phe Pro Arg	ap Leu Phe Met Ser	Tyr Phe Pro Arg
					100	105	110
<210> 50					Gly Leu Lys Tyr Gln Glu Gly Gly Val Glu Ser Ala Phe His Lys Thr	ly Val Glu Ser Ala	Phe His Lys Thr
<211> 348					1.15	120	125
15 <212> PRT	E.			. 15	Ser Thr Gly Ala Pro Ala Ala Ile Lys Lys Leu Tyr Gln Vel Lys Gly	le Lys Lys Leu Tyr	Gln Val Lys Gly
<213> Homo sapiens	no sapiens				130 135	140	
<220>.					Lys Lys Asn Ile Arg Ala Thr Glu Arg Ala Leu Asn Trp Asp Ser Phe	lu Arg Ala Leu Asn	Trp Asp Ser Phe
<221> Mac	<221> Macrophage capping protein	rotein			145 150	155	160
<222> (1)	(1)(348)				Asn Thr Gly Asp Cys Phe ile Leu Asp Leu Gly Gln Asn Ile Phe Ale	eu Asp Leu Gly Gln	Asn Ile Phe Ala
20 <223> Acc	Accession No. as of 10 Dec 2002; P40121	10 Dec 2002: P40.	121		165	170	175
<400> 50					Trp Cys Gly Gly Lys Ser Asn Ile Leu Glu Arg Asn Lys Ala Arg Asp	le Leu Glu Arg Asn	Lys Ala Arg Asp
				•	180	185	190
Met Tyr T	Met Tyr Thr Ala Ile Pro Gln Ser Gly Ser Pro Phe Pro	Ser Gly Ser Pro	Phe Pro Gly Ser Val		Leu Ala Leu Ala Ile Arg Asp Ser Glu Arg Gln Gly Lys Ala Gln Val	er Glu Arg Gln Gly	Lys Ala Gln Val
1	ĸ	10	. 35		195	200	205

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Glu ile Val Thr Asp Gly Glu Glu Pro Ala Glu Met Ile Gln Val Leu	<2220>
210 215 220	<221> Annexin I
Gly Pro Lys Pro Ala Leu Lys Glu Gly Asn Pro Glu Glu Asp Leu Thr	<222> (1). (346)
225 230 235 240	<223> Accession No. as of 10 Dec 2002: P04083
5 Ala Asp Lys Ala Asn Ala Gin Ala Ala Ala Leu Tyr Lys Val Ser Asp	5 <400> 51
. 245 250 255	
Ala Thr Gly Gln Met Asn Leu Thr Lys Val Ala Asp Ser Ser Pro Phe	Met Ala Met Val Ser Glu Phe Leu Lys Gln Ala Try Phe Ile Glu Asn
260 265 270	1 5 10 15
Ala Leu Glu Leu Leu Ile Ser Asp Asp Cys Phe Val Leu Asp Asn Gly	Glu Glu Glu Tyr Val Gln Thr Val Lys Ser Ser Lys Gly Gly Pro
	10 20 25 30
Leu Cys Gly Lys Ile Tyr Ile Trp Lys Gly Arg Lys Ala Asn Glu Lys	Gly Ser Ala Val Ser Pro Tyr Pro Thr Phe Asn Pro Ser Ser Asp Val
290 295 300	35 40
Glu Arg Gln Ala Ala Leu Gln Val Ala Glu Gly Phe Ile Ser Arg Met	Ala Ala Leu His Lys Ala Ile Met Val Lys Gly Val Asp Glu Ala Thr
305 310 315 320	90 55 09
15 Gln Tyr Ala Pro Asn Thr Gln Val Glu 11e Leu Pro Gln Gly Arg Glu	15 Ile Ile Asp Ile Leu Thr Lys Arg Asn Asn Ala Gln Arg Gln Gln Ile
325 . 330 335	65 70 75 80
Ser Pro Ile Phe Lys Gln Phe Lys Asp Trp Lys	Lys Ala Ala Tyr Leu Gin Glu Thr Gly Lys Pro Leu Asp Glu Thr Leu
340 345	56 06 58
	Lys Lys Ala Leu Thr Gly His Leu Glu Glu Val Val Leu Ala Leu Leu
	20 100 105 110
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<211> 346	115 120 125
<212> PRT	Gly Leu Gly Thr Asp Glu Asp Thr Leu ile Glu ile Leu Ala Ser Arg
<213> Homo sapiens	130 135 140

WO 2004/055519			PCT/EP2003/014057	4057	WO 2004/055519		144	PCT/EP2003/014057
	**	155/335				156/335		
Thr Asn Ly	Thr Asn Lys Glu Ile Arg Asp Ile Asn Arg Val Tyr Arg	sn Arg Val Tyr ?	Arg Glu Glu Leu		Lys ile Leu V	Lys Ile Leu Val Ala Leu Cys Gly Gly Asn	y Asn	
145	150	155	160		m	340 . 345	'n	
Lys Arg As	Lys Arg Asp Leu Ala Lys Asp Ile Thr Ser Asp Thr Ser	hr Ser Asp Thr S	Ser Gly Asp Phe					
	165	170	175					
5 Arg Asn Ale	Arg Asn Ala Leu Leu Ser Leu Ala Lys Gly Asp Arg Ser	ys Gly Asp Arg S	Ser Glu Asp Phe		5 <210> 52			•
	180	185	190		<211> 469			
Gly Val Ası	Gly Val Asn Glu Asp Leu Ala Asp Ser Asp Ala Arg Ala	er Asp Ala Arg A	ıla beu Tyr Glu		<212> PRT			
195	5 200	8	205		<213> Homo sapiens	piene		
· Ala Gly Glı	Ala Gly Glu Arg Arg Lys Gly Thr Asp Val Asn Val Phe	sp Val Asn Val P	he Asn Thr Ile		<220>			
10 .210	215	220			10 <221> Keratin	<221> Keratin, type II cytoskeletal	7 1	
Leu Thr Th	Leu Thr Thr Arg Ser Tyr Pro Gln Leu Arg Arg Val Phe	su Arg Arg Val P	he Gln Lys Tyr	•	<222> (1)(469)	(69)		
225	230	235	240		<223> Access1	Accession No. as of 10 Dec 2002; P08729	002: P08729	
Thr Lys Tyr	Thr Lys Tyr Ser Lys His Asp Met Asn Lys Val Leu Asp	sn Lys Val Leu A	sp heu Glu heu		<400> 52			
	245	250	255					
15 Lys Gly Asp	Lys Gly Asp Ile Glu Lys Cys Leu Thr Ala Ile Val Lys	ır Ala Ile Val Lı	ys Cys Ala Thr		15 Met Ser Ile Hi	Met Ser 11e His Phe Ser Ser Pro Val Phe Thr Ser Arg Ser Ala Ala	Phe Thr Ser Arg Ser	ila Ala
	260 265	55	270		Н	us.	10	15
Ser Lys Pro	Ser Lys Pro Ala Phe Phe Ala Glu Lys Leu His Gln Ala	s Leu His Gln A	la Met Lys Gly		Phe Ser Gly Ar	Phe Ser Gly Arg Gly Ala Gln Val Arg Leu Ser Ser Ala Arg Pro Gly	Leu Ser Ser Ala Arg	ro Gly
. 275	280	22	285		20	25	30	
Val Gly Thr	Val Gly Thr Arg His Lys Ala Leu Ile Arg Ile Met Val	e Arg Ile Met Ve	al Ser Arg Ser		Gly Leu Gly Se	Gly Leu Gly Ser Ser Leu Tyr Gly Leu Gly Ala Ser Arg Pro Arg	Leu Gly Ala Ser Arg	ro Arg
20 290	295	300			20 35	. 40	រ ភ ់ ទាំ	
Glu ile Asp	Glu ile Asp Met Asn Asp ile Lys Ala Phe Tyr Gln Lys	a Phe Tyr Gln Ly	ys Met Tyr Gly		Val Ala Val Arg	Val Ala Val Arg Ser Ala Tyr Gly Gly Pro Val Gly Ala Gly Ile Arg	Pro Val Gly Ala Gly 1	le Arg
305	310	315	320		. 50	. 10	09	
Ile Ser Leu	. Ile Ser Leu Cys Gin Ala Ile Leu Asp Glu Thr Lys Gly	p Glu Thr Lys Gl	ly Asp Tyr Glu		Glu Val Thr Ile	Glu Val Thr Ile Asn Gln Ser Leu Leu Ala Pro Leu Arg Leu Asp Ala	Ala Pro Leu Arg Leu A	sp Ala
	325	330	335		65	70	75	80

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Asp Pro Ser Leu Gln Arg Val Arg Gln Glu Glu Ser Glu	u Gln Ile Lys	Lys Cys Ser Arg Ala Glu Ala Glu Ala Trp Tyr Gln Thr Lys Phs Glu	s Phe Glu
	5.5	275 280 285	
Thr Leu Asn Asn Lys Phe Ala Ser Phe Ile Asp Lys Val	.1 Arg Phe Leu	Thr Leu Gln Ala Gln Ala Gly Lys His Gly Asp Asp Leu Arg Asn Thr	g Asn Thr
100 105	110	290 295 300	
5 Glu Gln Gln Asn Lys Leu Leu Glu Thr Lys Trp Thr Leu Leu Gln Glu	u Leu Gln Glu	5 Arg Asn Glu Ile Ser Glu Met Asn Arg Ala Ile Gln Arg Leu Gln Ala	u Gln Ala
115 120 125		305 310 315	320
Gln Lys Ser Ala Lys Ser Ser Arg Leu Pro Asp Ile Phe	e Glu Ala Gln	Glu ile Asp Asn ile Lys Asn Gln Arg Ala Lys Leu Glu Ala Ala ile	a Ala Ile
130 135 140		325 330	335
ile Ala Gly Leu Arg Gly Gln Leu Glu Ala Leu Gln Val	l Asp Gly Gly	Ala Glu Ala Glu Glu Arg Gly Glu Leu Ala Leu Lys Asp Ala Arg Ala	a Arg Ala
10 145 150 155	160	10 340 345 350	
Arg Leu Glu Gln Gly Leu Arg Thr Met Gln Asp Vel Vel Glu Asp Phe	I Glu Asp Phe `	Lys Gin Giu Giu Leu Giu Ala Ala Leu Gin Arg Ala Lys Gin Asp Met	л Авр Мес
165 170	175	355 360 365	
Lys Asn Lys Tyr Glu Asp Glu Ile Asn Arg Arg Thr Ala Ala Glu Asn	a Ala Glu Asn	Ala Arg Gln Leu Arg Glu Tyr Gln Glu Leu Met Ser Val Lys Leu Ala	s Leu Ala
180 185	190	370 375 380	
15 Glu Phe Val Val Leu Lys Lys Asp Val Asp Ala Ala Tyr Met Ser Lys		15 Leu Asp Ile Glu Ile Ala Thr Tyr Arg Lys Leu Leu Glu Gly Glu Glu	dlu Glu
. 195 200 205		385	400
Val Glu Leu Glu Ala Lys Val Asp Ala Leu Asn Asp Glu Ile Asn Phe	ı Ile Asn Phe	Ser Arg Leu Ala Gly Asp Gly Val Gly Ala Val Asn Ile Ser Val Met	. Val Met
. 210 215		. 405 410	415
Leu Arg Thr Leu Asn Glu Thr Glu Leu Thr Glu Leu Gln S	ser Gln Ile	Asn Ser Thr Gly Gly Ser Ser Ger Gly Gly Gly Ile Gly Leu Thr Leu	Thr Leu
20 225 · 230 235	240	20 420 425 430	
Ser Asp Thr Ser Val Val Leu Ser Met Asp Asn Ser Arg S	Ser Leu Asp	Gly Gly Thr Met Gly Ser Asn Ala Leu Ser Phe Ser Ser Ala Gly	: Ala Gly
245 . 250	255	435 440 445	
Leu Asp Gly Ile Ile Ala Glu Val Lys Ala Gln Tyr Glu Glu Met Ala	Glu Met Ala	Pro Gly Leu Leu Lys Ala Tyr Ser Ile Arg Thr Ala Ser Ala Ser Arg	Ser Arg
. 260 265	270	450 455 460	

3/014057 WO 2004/055519 160/335 PCT/EP2003/014057	Pro Gly Tyr Wet Arg Met Glu Gly Met Lys Gly Cys Pro Ala Val Leu	56 06 58	Pro Ile Asp His Val Tyr Gly Thr Leu Gly Ile Val Gly Ale Thr Thr	Tyr Ser Asp Ala	115 120 125	Lys Gly Ser Phe Thr Tyr Phe Ala Pro Ser Asn Glu Ala Trp Asp Asn	Leu Asp Ser Asp Ile Arg Arg Gly Leu Gor and Hall Ser Asp Ile Arg Arg Gly Leu Gor and Hall Ser Asp Ile Arg Arg Gly Leu Gor and Hall Ser Asp Ile Arg Arg Gly Leu Gly Gor and Hall Ser Asp Ile Arg Arg Gly Leu Gly Gor and Hall Ser Asp Ile Arg Arg Gly Feu Gly Gor and Hall Ser Asp Ile Arg Arg Gly Feu Gly Gor and Hall Ser Asp Ile Arg Arg Gly Feu Gly Gor and Hall Ser Asp Ile Arg Arg Gly Feu Gly Gor and Hall Ser Asp Ile Arg Arg Gly Feu Gly Gor and Hall Ser Asp Ile Arg Arg Gly Feu Gly Gor and Hall Ser Asp Ile Arg Arg Gly Feu Gly Gor and Hall Ser Asp Ile Arg Arg Gly Feu Gly Gor and Hall Ser Asp Ile Arg Arg Gly Feu Gly Gor and Hall Ser Asp Ile Arg Arg Gly Feu Gly Gor and Hall Ser Asp Ile Arg Arg Gly Feu Gly Gor and Hall Ser Asp Ile Arg Arg Gly Feu Gly Gor and Hall Ser Asp Ile Arg Arg Gly Feu Gly Gor and Hall Ser Asp Ile Arg Arg Gly Feu Gly Gor and Hall Ser Asp Ile Arg Arg Gly Feu Gly Gor and Hall Ser Asp Ile Arg Arg Gly Gor Asp Ile Arg Gly Gor Asp Ile Arg Gly Gor As	10 145 150 150 155 150 155 160 165 160 160 160 160 160 160 160 160 160 160	Leu Leu Asn Ale Leu His Ser His Met Ile Asn Lys Arg, Met Leu Thr	165 170 175	Lys Asp Leu Lys Asn Gly Met Ile Ile Pro Ser Met Tyr Asn Asn Leu	180 185 190	15 Gly Leu Phe Ile Asn His Tyr Pro Asn Gly Val Val Thr Val Asn Cys	195 200 205	Ale Arg Ile Ile His Gly Asn Gln Ile Ala Thr Asn Gly Val Val His	210 215 220	Val Ile Asp Arg Val Leu Thr Gln Ile Gly Thr Ser Ile Gln Asp Phe	20 225 230 235 240	ile Glu Ala Glu Asp Asp Leu Ser Ser Phe Arg Ala Ala Ala Ile Thr	245 250 255	Ser Asp Ile Leu Glu Ala Leu Gly Arg Asp Gly His Phe Thr Leu Phe	260 265 270		
WO 2004/055519 PCT/EP2003/014057	Arg Ser Ala Arg Asp	465			<211> 836 <210, non		<213> Homo sapiens - <220>	. 10 <221> Osteoblast specific factor 2 precursor	<222> (1)(836)	<223> Accession No. as of 10 Dec 2002: Q15063	<400> 53		15 Wet Ile Pro Phe Leu Pro Met Phe Ser Leu Leu Leu Leu Leu Ile Val	1 5 10 15	Asn Pro lle Asn Ala Asn Asn His Tyr Asp Lys lle Leu Ala His Ser	20 25 30	Arg Ile Arg Gly Arg Asp Gln Gly Pro Asn Val Cys Ala Leu Gln Gln	20 35 40 45	ile beu Gly Thr Lys Lys Tyr Phe Ser Thr Cys Lys Asn Trp Tyr	90 25 09	. Lys Lys Ser Ile Cys Gly Gln Lys Thr Thr Val Leu Tyr Glu Cys Cys	65 70 75 80		

	WO 2004/055519		PCT/FP2003/014057	WO JUNIOREE10	
		163/335		٠	164/335
	Arg Gly Ser Thr Phe Lys Glu Ile	ile Pro Val Thr Val Tyr Thr Thr Lys	The Lys		
	099	665 670			
	ile ile Thr Lys Val Val Glu Pro Lys ile Lys Val ile Glu Gly Ser	Pro Lys Ile Lys Val Ile Glu	Gly Ser	<210> 54	
	675	680 685		<211> 687	
5	Leu Gln Pro Ile Ile Lys Thr Glu	ilu Gly Pro Thr Leu Thr Lys Val Lys		5 <212> PRT	
	690 695	700		<213> Homo sapiens	
	ile Glu Gly Glu Pro Glu Phe Arg	rg beu ile bys Glu Gly Glu Thr	Thr Ile	<220>	
	710	715	720	<221> Protein-glutamine gamma-glutamyltransferase	lutamyltransferase
	Thr Glu Val Ile His Gly Glu Pro	ro ile ile Lys Lys Tyr Thr Lys ile	Lys ile	<222> (1)(687)	
21	725	730	735	10 <223> Accession No. P21980	
	ile Asp Gly Val Pro Val Glu ile	le Thr Glu Lys Glu Thr Arg Glu Glu	פוח פוח	<400> 54	
	740	745 750			
	Arg ile ile Thr Gly Pro Glu ile	le Lys Tyr Thr Arg Ile Ser Thr Gly	тар С1у	Met Ala Glu Glu Leu Val Leu Glu Arg Cys Asp Leu Glu L	Arg Cys Asp Leu Glu I
	755	760 765			10
15	Gly Gly Glu Thr Glu Glu Thr Leu Lys Lys Leu Leu Gln Glu Glu Val	eu Lys Lys Leu Leu Gln Glu		15 Aen Gly Arg Asp His His Thr Ala Asp Leu Cys Arg Glu L	Asp Leu Cys Arg Glu L
	770 077	780			25 3
	Thr Lys Val Thr Lys Phe 11e Glu Gly Gly Asp Gly His Leu Phe Glu	lu Gly Gly Asp Gly His Leu	Phe Glu	Val Arg Arg Gly Gln Pro Phe Trp Leu Thr Leu His Phe G	teu Thr beu His Phe G
	785 790	79,5	900	35 40	45
	Asp Glu Glu Ile Lys Arg Leu Leu Gln Gly Asp Thr Pro Val Arg Lys	eu Gln Gly Asp Thr Pro Val	Arg Lys	Aen Tyr Glu Ala Ser Vel Asp Ser Leu Thr Phe Ser Val V	Leu Thr Phe Ser Val V
70	808	810	815 20	50 55	. 09
	Leu Gin Ala Asn Lys Lys Val Gin Gly Ser Arg Arg Arg Leu Arg Glu	in Gly Ser Arg Arg Arg Leu	Arg Glu	Pro Ala Pro Ser Gln Glu Ale Gly Thr Lys Ale Arg Phe P	Thr Lys Ala Arg Phe P
	820	830		65 70	75
•	Gly Arg Ser Gln			Asp Ala Val Glu Glu Gly Asp Trp Thr Ala Thr Val Val A	Thr Ala Thr Val Val A
				88 SC	06

Glu Leu Glu Thr

15

Glu Lys Leu Val

30

Phe Glu Gly Arg

45

Val Val Thr Gly

Phe Pro Leu Arg

Val Asp Gln Gln

95

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	WO 2004/055519		PCT/EP2003/014057		WO 2004/055519		PCT/EP2003/014057
		165/335				166/335	-
	Asp Cys Thr Leu Ser Leu Gln Leu Thr Thr Pro Ala Asn		Ala Pro Ile	. ,	Arg Cys Leu Gly Ile	Arg Cys Leu Gly Ile Pro Thr Arg Val Val Thr Asn Tyr Asn Ser Ala	: Asn Tyr Asn Ser Ala
	100	105	. 011		290	295	300
	Gly Leu Tyr Arg Leu Ser Leu Glu Ala Ser Thr Gly Tyr		Gln Gly Ser		His Asp Gln Asn Ser	His Asp Gln Asn Ser Asn Leu Leu Ile Glu Tyr Phe Arg Asn Glu Phe	. Phe Arg Asn Glu Phe
•	115	120 . 125			305	310 315	320
Ŋ	Ser Phe Val Leu Gly His Phe Ile Leu Leu Phe Asn Ala		Trp Cys Pro	'n		Gly Glu Ile Gln Gly Asp Lys Ser Glu Met Ile Trp Asn Phe His Cys	Trp Asn Phe His Cys
	130 135	140			325	330	335
	Ala Asp Ala Val Tyr Leu Asp Ser Glu Glu Glu Arg Gln Glu Tyr Val	r Glu Glu Glu Arg Gln (Glu Tyr Val		Trp Val Glu Ser Trp	Trp Val Glu Ser Trp Met Thr Arg Pro Asp Leu Gln Pro Gly Tyr Glu	Gln Pro Gly Tyr Glu
	145 .150	155	160		340	345	350
	Leu Thr Gln Gln Gly Phe Ile Tyr Gln Gly Ser Ala Lyg Phe Ile Lys	r Gln Gly Ser Ala Lys i	Phe ile Lys		Gly Trp Gln Ala Leu	Gly Trp Gln Ala Leu Asp Pro Thr Pro Gln Glu Lys Ser Glu Gly Thr	Lys Ser Glu Gly Thr
10	165	170	175	01	355	360	365
	Asn ile Pro Trp Asn Phe Gly Gln Phe Glu Asp Gly Ile Leu Asp ile	n Phe Glu Asp Gly Ile L	eu Asp Ile		Tyr Cys Cys Gly Pro	Tyr Cys Cys Gly Pro Val Pro Val Arg Ala Ile Lys Glu Gly Asp Leu	Lys Glu Gly Asp Leu
	180	185 1	190		370	375	380
	Cys Leu Ile Leu Leu Asp Val Asn Pro Lys Phe Leu Lys Asn Ala Gly	7 Pro Lys Phe Leu Lys A	isn Ala Gly		Ser Thr Lys Tyr Asp	Ser Thr Lys Tyr Asp Ala Pro Phe Val Phe Ala Glu Val Asn Ala Asp	Glu Val Asn Ala Asp
	195 200	205			385	390 395	400
15	Arg Asp Cys Ser Arg Arg Ser Ser Pro Val Tyr Val Gly Arg Val	: Pro Val Tyr Val Gly A	kg Val Val	15	val val Asp Trp Ile	Val Val Asp Trp ile Gln Gln Asp Asp Gly Ser Val His Lys Ser ile	Val His Lys Ser Ile
	210 215	220	·		405	410	415
	Ser Gly Met Val Asn Cys Asn Asp Asp Gln Gly Val Leu Leu Gly Arg	Asp Gln Gly Val Leu L	eu Gly Arg	•	Asn Arg Ser Leu Ile	Asn Arg Ser Leu Ile Val Gly Leu Lys Ile Ser Thr Lys Ser Val Gly	Thr Lys Ser Val Gly
	225 230	235	240		420	425	. 430
	Trp Asp Asn Asn Tyr Gly Asp Gly Val Ser Pro Met Ser Trp Ile Gly	. Val Ser Pro Met Ser To	rp Ile Gly		Arg Asp Glu Arg Glu	Arg Asp Glu Arg Glu Asp Ile Thr His Thr Tyr Lys Tyr Pro Glu Gly	Lys Tyr Pro Glu Gly
. 20	245	250	255	20	435	440	445
	Ser Val Amp Ile Leu Arg Arg Trp Lys Amn His Gly Cys Gln Arg Val	Lye Asn His Gly Cys Gl	In Arg Val	•	Ser Ser Glu Glu Arg	Ser Ser Glu Glu Arg Glu Ala Phe Thr Arg Ala Asn His Leu Asn Lys	Asn His Leu Asn Lys
	260	265 27	270		450	455	460
	Lys Tyr Gly Gln Cys Trp Val Phe Ala Ala Val Ala Cys Thr Val Leu	Ala Ala Val Ala Cys Th	hr Val Leu		Leu Ala Glu Lys Glu	Leu Ala Glu Lys Glu Glu Thr Gly Met Ala Met Arg Ile Arg Val Gly	Arg ile Arg Val Gly
	275 280	285			465	470 475	480

WO 2004/055519 DCT-man-not not not not not not not not not not	
167/335	WO 2004/055519 FCT/RP2003/014057 168/335
Gln Ser Met Asn Met Gly Ser Asp Phe Asp Val Phe Ala His Ile Thr	Leu Lys Ala Val Lys Gly Phe Arg Asn Val 11e 11e Gly Pro Ala
	675 680 685
Asn Asn Thr Ala Glu Glu Tyr Val Cys Arg Leu Leu Leu Cys Ala Arg	
500 505 510	
Thr Val Ser Tyr Asn Gly Ile Leu Gly Pro Glu Cys Gly Thr Lys Tyr	5 <210> 55
515 520 525	<211> 204
Leu Leu Asn Leu Asn Leu Glu Pro Phe Ser Glu Lys Ser Val Pro Leu	<212> PRT
530 535 540	<213> Homo sapiens
Cys Ile Leu Tyr Glu Lys Tyr Arg Asp Cys Leu Thr Glu Ser Asn Leu	<220>
545 550 555 560	10 <221> Rho GDF-dissociation inhibitor 1
Ile Lys Val Arg Ala Leu Leu Val Glu Pro Val Ile Asn Ser Tyr Leu	<222> (1)(204)
565 570 575	<223> Accession No. as of 10 Dec 2002: P52565
Leu Ala Glu Arg Asp Leu Tyr Leu Glu Asn Pro Glu Ile Lys Ile Arg	<400> 55
580 585 590	
Ile Leu Gly Glu Pro Lys Gln Lys Arg Lys Leu Val Ala Glu Val Ser	15 Met Ala Glu Gin Glu Pro Thr Ala Glu Gln Leu Ala Gln Ile Ala Ala
209 600	1 5 10 15
Leu Gln Asn Pro Leu Pro Val Ala Leu Glu Gly Cys Thr Phe Thr Val	Glu Asn Glu Glu Asp Glu His Ser Val Asn Tyr Lys Pro Pro Ala Gln
610 615 620	20 25 30
Glu Gly Ala Gly Leu Thr Glu Glu Gln Lys Thr Val Glu Ile Fro Asp	Lys Ser Ile Gln Glu Ile Gln Glu Leu Asp Lys Asp Asp Glu Ser Leu
625 630 635 . 640	20 35 40 45
Pro Val Glu Ala Gly Glu Glu Val Lys Val Arg Met Asp Leu Leu Pro	Arg Lys Tyr Lys Glu Ala Leu Gly Arg Val Ala Val Ser Ala Asp
645 650 655	. 09 . 25 . 09
Leu His Met Gly Leu His Lys Leu Val Val Asn Phe Glu Ser Asp Lys	Pro Asn Val Pro Asn Val Val Thr Gly Leu Thr Leu Val Cys Ser
660 665 670	65 70 75 80

-	WO 2004/055519	169/335	PCT/EP2003/014057	WO 2004/055519 PCT/	PCT/EP2003/01
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	100	105	110		
'n	Lys.Ile Ser Phe Arg Va	Lys.Ile Ser Phe Arg Val Asn Arg Glu Ile Val Ser Gl	er Gly Met Lyg Tyr	5 Met Pro Thr Asn Gly Leu His Gln Val Leu Lys Ile Gln Phe Gly Leu	3ly Leu
	. 115	120 125	n	1 5 10 15	<u>s</u> 1
	ile Gin His Thr Tyr Ar	ile Gin His Thr Tyr Arg Lys Gly Val Lys Ile Asp Lys Thr Asp Tyr	s Thr Asp Tyr	. Val Asn Asp Thr Asp Arg Tyr Leu Thr Ala Glu Ser Phe Gly Phe Lys	the Lys
	. 130	135 140		20 25 30	
	Met Val Gly Ser Tyr Gl	Met Val Gly Ser Tyr Gly Pro Arg Ala Glu Glu Tyr Glu Phe Leu Thr		Val Asn Ala Ser Ala Pro Ser Leu Lys Arg Lys Gln Thr Trp Val Leu	al Leu
01	145 150	155	160	0 35 40 45	
	Pro Val Glu Glu Ala Pr	Pro Val Glu Glu Ala Pro Lys Gly Met Leu Ala Arg Gly Ser Tyr	/ Ser Tyr Ser	Glu Pro Asp Pro Gly Gln Gly Thr Ala Val Leu Leu Arg Ser Ser His	er His
	165	170		50 55 60	
	Ile Lys Ser Arg Phe Th	lie Lys Ser Arg Phe Thr Asp Asp Asp Lys Thr Asp His Leu Ser Trp	Leu Ser Trp	Leu Gly Arg Tyr Leu Ser Ala Glu Glu Asp Gly Arg Val Ala Cys Glu	ys Glu
	180	185		65 70 75	80
15	Glu Trp Asn Leu Thr Il	Glu Trp Asn Leu Thr Ile Lys Lys Asp Trp Lys Asp	51	3 Ala Glu Gln Pro Gly Arg Asp Cys Arg Phe Leu Val Leu Pro Gln Pro	ln Pro
	195	200		56 06 58	ю
				Asp Gly Arg Trp Val Leu Arg Ser Glu Pro His Gly Arg Phe Phe Gly	he Gly
	,			100 105 110	
	<210> 56			Gly Thr Glu Asp Gln Leu Ser Cys Phe Ala Thr Ala Val Ser Pro Ala	ro Ala
20	<211> 492		20	115 120. 125	
	<212> PRT			Glu Leu Trp Thr Val His Leu Ala Ile His Pro Gln Ala His Leu Leu	neg ne
	<213> Homo sapiens			130 135 140	
	<220>			Ser Val Ser Arg Arg fyr Val His Leu Cys Pro Arg Glu Asp Glu	p Glu
	<221> Fascin 2			145 150 155	160

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Met Ala Ala Asp Gly Asp Lys Pro Trp Gly Val Asp	Ala Leu Thr	Val Cys Met Lys Lys Asn Gly Gln Leu Ala Ala Ile Ser Asp Phe Val
165 170	175	355 360 365
Leu Ile Phe Arg Ser Arg Arg Tyr Cys Leu Lys Ser	Cys Asp Ser Arg	Gly Lys Asp Glu Glu Phe Thr Leu Lys Leu Ile Asn Arg Pro Ile Leu
180 185	. 190	370 375 380
Tyr Leu Arg Ser Asp Gly Arg Leu Val Trp Glu Pro	Glu Pro Arg Ala	5 Val Leu Arg Gly Leu Asp Gly Phe Val Cys His His Arg Gly Ser Asn
195	205	385 390 395 400
Cys Tyr Thr Leu Glu Phe Lys Ala Gly Lys Leu Ala	. Phe Lys Asp Cys	Gln Leu Asp Thr Asn Arg Ser Val Tyr Asp Val Phe His Leu Ser Phe
210 215 220		405 , 410 415
Asp Gly His Tyr Leu Ala Pro Val Gly Pro Ala Gly ?	Thr Leu Lys Ala	Ser Asp Gly Ala Tyr Arg Ile Arg Gly Arg Asp Gly Gly Phe Trp Tyr
225 230 235	240	3 420 425 430
Gly Arg Asn Thr Arg Pro Gly Lys Asp Glu Leu Phe ?	Asp Leu Glu Glu	Thr Gly Ser His Gly Ser Val Cys Ser Asp Gly Glu Arg Ala Glu Asp
245 250	255	435 440 445
Ser His Pro Gln Val Val Leu Val Ala Ala Asn His P	Arg Tyr Val Ser	Phe Val Phe Glu Phe Arg Glu Arg Gly Arg Leu Ala Ile Arg Ala Arg
260. 265 .	270	450 455 460
Val Arg Gin Gly Val Asn Val Ser Ala Asn Gin Asp A	Asp Glu Leu Asp	ser Gly Lys Tyr Leu Arg Gly Gly Ala Ser Gly Leu Leu Arg Ala Asp
275 280 2	285	465 470 475 480
His Glu Thr Phe Leu Met Gln Ile Asp Gln Glu Thr L	Lys Lys Cys Thr	Ala Asp Ala Pro Ala Gly Thr Ala Leu Trp Glu Tyr
290 295 300		485 490
Phe Tyr Ser Ser Thr Gly Gly Tyr Trp Thr Leu Val T	Thr His Gly Gly	
305 310 315	320 20	
ile His Ala Thr Ala Thr Gln Val Ser Ala Asn Thr M	Met Phe Glu Met	<210> 57
325 330	335	<211> 165.
Glu Trp Arg Gly Arg Arg Val Ala Leu Lys Ala Ser A	Asn Gly Arg Tyr	<212> PRT
340 345	350	<213> Homo sapiens

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4222 (1)(165) 4222 (1)(165) 4200 57 Het Ale Ser Gly Val Gin Val Ale Aup Giu Val Cye Arg lie Phe Pyr 1
4222> (1)(165) 4222> (1)(165) 4222> (1)(165) 4223> Accession No. as of 29 August 2003; P19282 4400> 57 Asp Net Juy Val Cin Val Ala Asp Clu Val Cya Ary Ile Phe Tyr 1
4212> (11).(185) 4213> Accession No. as of 29 August 2003; P19282 4400> 57 1
4400- 57 Met Ala Ser City Vel Cin Vel Ala Asp Ciu Val Cya Arg Ile Phe Tyr. 1
1
1 5 10 15
1 5 10 15 Amp Note Lays Val Arg Lyo Cyo Ser Thir Pro Glu Wal Ile Pho Tyr 20 25 30 40 45 35 40 45 35 40 45 Thir Amp Pro Glu Glu Ile Lyo Lyo Cyo Ile Cyo Lau Ser Ala Amp Lyo Cyo Ile Cyo Leu Ser Ala Amp Lyo Cyo Ile Cyo Ile Cyo Leu Ser Ala Amp Lyo Cyo Ile Cyo Cyo Ile Cyo Ile Cyo Leu Ser Ala Amp Lyo Cyo Ile C
1
Amp Met Lys Val Arg Lys Cys Ser Thr Pro Glu Glu Ile Lyg Lyg Arg 20 25 30 40 43 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 46 40 46 40 46 40 46 40 46 40 46 40 46 40 46 40 46 40 40
157
1596 Lys Ala Val Ile Phe Cys Leu Ser Ala Asp Lys Lys Cys Ile Ile 35 40 45 45 45 40 45 45 40 45 45
135 40 45 45 46 45 45 46 45 46 45 46 45 46 46
Val Glu Glu Gly Lys Glu Ile Leu Val Gly Val Thr Ile 50 Thr Asp Pro. Phe Lys His Phe Val Gly Met Leu Pro Glu Lys Asp Cys 65 Arg Tyr Ala Leu Tyr Asp Ala Ser Phe Glu Thr Lys Glu Ser Arg Lys 85 61u Glu Leu Met Phe Phe Leu Trp Ala Pro Glu Leu Ala Pro Leu Lys 100 105 Ser Lys Met Ile Tyr Ala Ser Ser Lys Asp Ala Ile Lys Lys Phe 115 116 117 118 119 119 119 119
This Asp Pro Dhe Lys His Phe Val Gly Met Leu Pro Glu Lys Asp Cys 65 Arg Tyr Ala Leu Tyr Asp Ala Ser Phe Glu Thr Lys Glu Ser Arg Lys 85 Glu Glu Leu Met Phe Phe Leu Trp Ala Pro Glu Leu Ala Pro Leu Lys 100 Ser Lys Met Ile Tyr Ala Ser Ser Lys Asp Ala Ile Lys Lys Phe 115 116 117 118 118 119 119 119 110 110 110
15 The Asp Pro Phe Lys His Phe Val Gly Met Leu Pro Glu Lys Asp Cys Arg Tyr Ala Leu Tyr Asp Ala Ser Phe Glu Thr Lys Glu Ser Arg Lys Als Tyr Ala Leu Tyr Asp Ala Ser Phe Glu Thr Lys Glu Ser Arg Lys Glu Glu Leu Met Phe Phe Leu Trp Ala Pro Glu Leu Ala Pro Leu Lys 100 Ser Lys Met Ile Tyr Ala Ser Ser Lys Asp Ala Ile Lys Lys Phe 115 116 117 118 119 119 119 119 119 119
98
20
20
20
20
135 140 55

•	WO 2004/055519 175/	175/335	PCT/EP2003/014057		WO 2004/055519 176	PCT/EP2003/014057
	Leu Gly Arg Tyr Leu Ala Ala Asp Lys Asp Gly Asn Val		Thr Cys Glu		Gln Ser Cys Ale Gln Val Val Leu Gln Ala Ala Asn Glu Arg Asn val	iln Ala Ala Asn Glu Arg Asn vel
	55 70	75	80		260	265 270
	Arg Glu Val Pro Gly Pro Asp Cys Arg Phe Leu Ile Val		Ala His Asp		Ser Thr Arg Gln Gly Met Asp Leu Ser Ala Asn Gln Asp Glu Glu Thr	er Ala Asn Gln Asp Glu Glu Thr
	885	06	95		275 280	285
8	Asp Gly Arg Trp Ser Leu Gln Ser Glu Ala His Arg Arg		Tyr Phe Gly		5 Asp Gin Glu Thr Phe Gin Leu Glu Ile Asp Arg Asp Thr Lys Lys Cys	le Asp Arg Asp Thr Lys Lys Cys
	100	105	C		290 . 295	300
	Gly Thr Glu Asp Arg Leu Ser Cys Phe Ala Gln Thr Val		Ser Pro Ala		Ala Phe Arg Thr His Thr Gly Lys Tyr Trp Thr Leu Thr Ala Thr Gly	Yr Trp Thr Leu Thr Ala Thr Gly
	115 . 120	125			305 310	315 320
	Glu Lys Trp Ser Val His Ile Ala Met His Pro Gln Val		Asn Ile Tyr		Gly Val Gln Ser Thr Ala Ser Ser Lys Asn Ala Ser Cys Tyr Phe Asp	/8 Asn Ala Ser Cys Tyr Phe Asp
01	130 135	140		01		330 335
	Ser Val Thr Arg Lys Arg Tyr Ala His Leu Ser Ala Arg		Pro Ala Asp		ile Glu Trp Arg Asp Arg Arg ile Thr Leu Arg Ala Ser Asn Gly Lys	r Leu Arg Ala Ser Asn Gly Lys
	145 150	155	160		340 34	345 350
-	Glu ile Ala Vel Asp Arg Asp Val Pro Trp Gly Val Asp Ser Leu ile	o Trp Gly Val Asp Ser	Leu Ile		Phe Val Thr Ser Lys Lys Asn Gly Gln Leu Ala Ala Ser Val	n Leu Ala Ala Ser Val Glu Thr
	165	170	175		355 360	365
15 3	Thr Leu Ala Phe Gin Asp Gin Arg Tyr Ser Val Gin Thr Ala Asp His	r Ser Val Gln Thr Ala	Абр Нів.	15	Ala Gly Asp Ser Glu Leu Phe Leu Met Lys Leu Ile Asn Arg Fro Ile	t Lys Leu lle Asn Arg Pro Ile
	180 . 185	5 190		٠	370 375	380
7	Arg Phe Leu Arg His Asp Gly Arg Leu Val Ala Arg Pro Glu Pro Ala	u Val Ala Arg Pro Glu	Pro Ala		Ile Val Phe Arg Gly Glu His Gly Phe Ile Gly Cys Arg Lys Val Thr	e Ile Gly Cys Arg Lys Val Thr
	195 200	205			385 390	395 400
-	Thr Gly Tyr Thr Leu Glu Phe Arg Ser Gly Lys Val Ala		Phe Arg Asp		Gly Thr Leu Asp Ala Asn Arg Ser Ser Tyr Asp Val Phe Gln Leu Glu	r Tyr Asp Val. Phe Gln Leu Glu
70	210 215	220		. 50		410 415
U	Cys Glu Gly Arg Tyr Leu Ala Pro Ser Gly Pro Ser Gly Thr Leu Lys	: Gly Pro Ser Gly Thr	Leu Lys		Phe Asn Asp Gly Ala Tyr Asn Ile Lys Asp Ser Thr Gly Lys Tyr	3 Asp Ser Thr Gly Lys Tyr Trp
7	225 230	235	240	-	420 425	430
¥	Ala Gly Lys Ala Thr Lys Val Gly Lys Asp Glu Leu Phe Ala Leu Glu	Asp Glu Leu Phe Ala	ren Glu		Thr Val Gly Ser Asp Ser Ala Val Thr Ser Ser Gly Asp Thr Pro Val	Ser Ser Gly Asp Thr Pro Val
	245	250	255	•	435 440	445

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Asp Phe Phe Glu Phe Cys Asp Tyr Asn Lys Val Ala Ile Lys Vel	Gly Arg Phe Trp Asp Tyr Leu Arg Trp Vel Gln Thr Leu Ser Glu Gln
450 455 460	50 55 60
Gly Gly Arg Tyr Leu Lys Gly Asp His Ala Gly Val Leu Lys Ala Ser	Val Gln Glu Leu Leu Ser Ser Gln Val Thr Gln Glu Leu Arg Ala
465 470 475 480	65 70 75 80
5 Ala Glu Thr Val Asp Pro Ala Ser Leu Trp Glu Tyr	5 Leu Met Asp Glu Thr Met Lya Glu Leu Lya Ala Tyr Lya Ser Glu Leu
485	85 90 95
	Glu Glu Glu Ieu Thr Pro Val Ala Glu Glu Thr Arg Ala Arg Leu Ser
	100 105 . 110
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Met Lys Val Leu Trp Ala Ala Leu Leu Val Thr Phe Leu Ala Gly Cys	Ser Ala Ile Arg Glu Arg Leu Gly Pro Leu Val Glu Gln Gly Arg Val
20 1 5 10 15	20 195 , 200 205
Gln Ala Lys Val Glu Gln Ala Val Glu Thr Glu Pro Glu Pro Glu Leu	Arg Ala Ala Thr Val Gly Ser Leu Ala Gly Gln Pro Leu Gln Glu Arg
20 25 30	210 215 220
Arg Gln Gln Thr Glu Trp Gln Ser Gly Gln Arg Trp Glu Leu Ala Leu	Ala Gln Ala Trp Gly Glu Arg Leu Arg Ala Arg Met Glu Glu Met Gly
35 40 45	225 230 235 240

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WO 2004/055519	200,000	PCT/EP2003/014057	WO 2004/055519	PCT/EP2003/014057
	200/21		180/335	
Ser Arg Th	Ser Arg The Arg Asp Arg Leu Asp Glu Val Lys Glu Gln Va.	Val Ala Glu	Gly Thr Val Thr Vel Arg Tyr Ala Pro Ser Glu Ala Gly Leu His Glu	/ Leu His Glu
	245 250	255	20 25	30
Val Arg Al	Val Arg Ala Lys Leu Glu Glu Gln Ala Gln Gln Ile Arg Leu	Leu Gln Ala	Met Asp Ile Arg Tyr Asp Asn Met His Ile Pro Gly Ser Pro Leu Gln	Fro Leu Glu
	260 265 270		35 40 45	
5 Glu Ala Phe	Gln Ala Arg Leu Lys Ser Trp Phe Glu Pro	Leu Val Glu	5 Phe Tyr Val Asp Tyr Val Asn Cys Gly His Val Thr Ale Tyr Gly Pro	Tyr Gly Pro
275	280		90 55 60	
Asp Met Gl	Asp Met Gln Arg Gln Trp Ala Gly Leu Val Glu Lys Val Gln	Gin Ala Ala	Gly Leu Thr His Gly Val Val Asn Lys Pro Ala Thr Phe Thr Val Asn	Thr Val Asn
290	295 300		65 .70 75	. 08
Val Gly Th	Val Gly Thr Ser Ala Ala Pro Val Pro Ser Asp Asn His		Thr Lys Asp Ala Gly Glu Gly Gly Leu Ser Leu Ala Ile Glu Gly Pro	Glu Gly Pro
10 305	310 315	10	06 88 0	95
			Ser Lys Ala Glu Ile Ser Cys Thr Asp Asn Gln Asp Gly Thr Cys Ser	Thr Cys Ser
			100 105	110
<210> 60			Val Ser Tyr Leu Pro Val Leu Pro Gly Asp Tyr Ser Ile Leu Val Lys	Leu Val Lys
<211> 838	,		115 120 125	
15 <212> PRT		15	5 Tyr Asn Glu Gln His Val Pro Gly Ser Pro Phe Thr Als Arg Val Thr	Arg Val Thr
<213> Homo sapiens	. sapiens		130 135 140	
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	,		180 185 1.	
Met Pro Ser	Met Pro Ser Gly Lys Val Ala Gin Pro Thr Ile Thr Asp Asn Lys Asp	буз Авр	Leu Arg Asn Gly His Val Gly Ile Ser Phe Val Pro Lys Glu Thr Gly	Glu Thr Gly
1	. 10	15	205 200 205	

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Glu His Leu Val His Val Lys Lys Asn Gly Gln His Val Ala	s Lys Asn Gly Gln His Val	Ala Ser Ser	His Thr Val Ser Val Lys Tyr Lys Gly Gln His Val Pro Gly Ser Pro
210 215	5 220		405 410 415
Pro ile Pro Val Val ile Ser Gln Ser Glu ile Gly Asp Ala Ser Arg	r Gln Ser Glu Ile Gly Asp	Ala Ser Arg	Phe Gin Phe Thr Val Gly Pro Leu Gly Glu Gly Gly Ala His Lys Val
225 , 230	235	240	420 425 430
5 Val Arg Val Ser Gly Gln Gly Leu His Glu Gly His Thr Phe Glu Pro	y Leu His Glu Gly His Thr	Phe Glu Pro	5 Arg Ala Gly Gly Pro Gly Leu Glu Arg Ala Glu Ala Gly Val Pro Ala
245	250	255	435. 440 445
Ala Glu Phe Ile Ile Asp Thr Arg Asp Ala Gly Tyr Gly Gly Leu Ser	r Arg Asp Ala Gly Tyr Gly	Gly Leu Ser	Glu Phe Ser Ile Trp Thr Arg Glu Ala Gly Ala Gly Gly Leu Ala Ile
260	265	270	450 455 460
Leu Ser 11e Glu Gly Pro Ser Lys Val Asp Ile Asn Thr	r Lys Val Asp Ile Asn Th r	Glu Asp Leu	Ala Val Glu Gly Pro Ser Lys Ala Glu Ile Ser Phe Glu Asp Arg Lys
275	280 285		10 465 470 475 480
Glu Asp Gly Thr Cys Arg Val Thr Tyr Cys Pro Thr Glu	1 Thr Tyr Cys Pro Thr Glu	Pro Gly Asn	Asp Gly Ser Cys Gly Val Ala Tyr Val Val Gln Glu Pro Gly Asp Tyr
290 295	300		485 490 495
Tyr lle lle Asn lle Lys Phe Ala Asp Gln His Val Pro	e Ala Asp Gln His Val Pro	Gly Ser Pro	Glu Val Ser Val Lys Phe Asn Glu Glu His Ile Pro Asp Ser Pro Phe
305 310	315	320	. 500 505 510
5 Phe Ser Val Lys Val Thr Gly Glu Gly Arg Vel Lys Glu Ser	y Glu Gly Arg Val Lys Glu	Ser Ile Thr	15 Val Val Pro Val Ala Ser Pro Ser Gly Asp Ala Arg Arg Leu Thr Val
325	330	335	515 520 525
Arg Arg Arg Arg Ala Pro Ser Val Ala Asn Val Gly Ser His Cys Asp	r Val Ala Asn Val Gly Ser	His Cys Asp	Ser Ser Leu Gln Glu Ser Gly Leu Lys Val Asn Gln Pro Ala Ser Phe
340	345	350	530 535 540
Leu Ser Leu Lys Ile Pro Glu Ile Ser Ile Gln Asp Met	u ile Ser ile Gin Asp Met	Thr Ala Gln	Ala Val Ser Leu Asn Gly Ala Lys Gly Ala Ile Asp Ala Lys Val His
355	360 365		20 545 550 555 S60
Val Thr Ser Pro Ser Gly Lys Thr His Glu Ala Glu Ile Val	s Thr His Glu Ala Glu Ile	Val Glu Gly	Ser Pro Ser Gly Ala Leu Glu Glu Cys Tyr Val Thr Glu Ile Asp Gln
370 375	380		575 570 575
Glu Asn His Thr Tyr Cys Ile Arg Phe Val Pro Ala Glu Met Gly Thr	e Arg Phe Val Pro Ala Glu	Met Gly Thr	Amp Lys Tyr Ala Val Arg Phe Ile Pro Arg Glu Amn Gly Val Tyr Leu
385 390	395	400	

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### PCT/EP2003/014057 ###################################	### PCT/EP2003/014057 184/335 Val His Gly Pro Arg Thr Pro Cys Glu Glu Ile Leu Val Lys His Val 785 790 795 800 Gly Ser Arg Leu Tyr Ser Val Ser Tyr Leu Leu Lys Asp Lys Gly Glu 805 810 820 825 830 Tyr Thr Leu Val Val Pro 825 830 1yr Arg Val Val Val Pro
11e Asp Val Lys Phe Asn Gly Thr His Ile Pro Gly Ser Pro Phe Lys 605 605 605 11e Arg Val Gly Glu Pro Gly His Gly Gly Asp Pro Gly Leu Val Ser 620 620 Ala Tyr Gly Ala Gly Leu Glu Gly Gly Val Thr Gly Asn Pro Ala Glu 615 640 Phe Val Val Asn Thr Ser Asn Ala Gly Ala Gly Ala Leu Ser Val Thr 655 655 655 655 Ile Asp Gly Pro Ser Lys Val Lys Met Asp Cys Gln Glu Gys Pro Glu 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 665 66	18 Gly Pro Arg Thr Pro Cys Glu Glu Ile Leu Val Lys His Val 790 795 800 er Arg Leu Tyr Ser Val Ser Tyr Leu Leu Lys Asp Lys Gly Glu 805 810 815 hr Leu Val Val Lys Trp Gly Asp Glu His Ile Pro Gly Ser Pro 820 825 830 Fg Val Val Val Pro
11e Arg Val Gly Glu Pro Gly His Gly Gly Asp Pro Gly Leu Val Ser 610 Ala Tyr Gly Ala Gly Leu Glu Gly Gly Val Thr Gly Asn Pro Ala Glu 625 Ala Tyr Gly Ala Gly Leu Glu Gly Gly Val Thr Gly Asn Pro Ala Glu 625 Phe Val Val Asn Thr Ser Asn Ala Gly Ala Leu Ser Val Thr 645 656 11e Asp Gly Pro Ser Lys Val Lys Met Asp Cys Gln Glu Gys Pro Glu 666 6670 670 670 670 670 670 6	790 795 800 er Arg Leu Tyr Ser Val Ser Tyr Leu Leu Luu Lys Asp Lys Gly Glu 805 815 hr Leu Val Val Lys Trp Gly Asp Glu His Ile Pro Gly Ser Pro 820 825 830 rg Val Val Val Pro
11e Arg Val Gly Gly His Gly Gly His Gly Gly Leu Val Ser 610 615 620 Ala Tyr Gly Ala Gly Leu Glu Gly Gly Val Thr Gly Asn Pro Ala Glu 640 Fhe Val Val Asn Thr Ser Asn Ala Gly Ala Leu Ser Val Thr 655 656 655 Ile Asp Gly Pro Ser Lys Val Lys Met Asp Cys Gln Glu Gys Pro Glu 660 665 670 10	### Arg Leu Tyr Ser Val Ser Tyr Leu Leu Lys Asp Lys Gly Glu ### 805 ### 815 ### 1. Leu Val Val Lys Trp Gly Asp Glu His Ile Pro Gly Ser Pro ### 820 ### 830 ### 830 ### 835 ### 835
Ala Tyr Gly Ala Gly Leu Glu Gly Gly Val Thr Gly Asn Pro Ala Glu 625 626 630 635 640 Phe Val Val Asn Thr Ser Asn Ala Gly Ala Leu Ser Val Thr 645 645 650 655 Ile Asp Gly Pro Ser Lys Val Lys Met Asp Cys Gln Glu Cys Pro Glu 660 660 665	815 tr Leu Val Val Lys Trp Gly Asp Glu His Ile Pro Gly Ser Pro 820 825 830 rg Val Val Val Pro 835
Ala Tyr Gly Ala Gly Leu Glu Gly Gly Val Thr Gly Asn Pro Ala Glu 625 626 640 640 645 646 646 646 646 647 645 650 655 640 645 650 655 650 655 11e Asp Gly Pro Ser Lys Val Lys Met Asp Cys Gln Glu Cys Pro Glu 660 666 670 10	hr Leu Val Val Lys Trp Gly Asp Glu His Ile Pro Gly Ser Pro 820 825 830 Eg Val Val Val Pro
625 630 635 640 Phe Val Val Asn Thr Ser Asn Ala Gly Ala Leu Ser Val Thr 645 650 655 Ile Asp Gly Pro Ser Lys Val Lys Met Asp Cys Gln Glu Cys Pro Glu 660 665 670	
Phe Val Val Asn Thr Ser Asn Ala Gly Ala Leu Ser Val Thr 645 650 655 Ile Asp Gly Pro Ser Lys Val Lys Met Asp Cys Gln Glu Cys Pro Glu 660 665	rg Val Val Pro 835
645 650 655 Ile Asp Gly Pro Ser Lys Val Lys Met Asp Cys Gln Glu Cys Pro Glu 660 665 670	835
Ile Asp Gly Pro Ser Lys Val Lys Met Asp Cys Gln Glu Cys Pro Glu 660 665 670	
. 029 639 099	
Gly Tyr Arg Val Thr Tyr Thr Pro Met Ala Pro Gly Ser Tyr Leu Ile	61
675 680 685 <211>	433
Ser lle Lys Tyr Gly Gly Pro Tyr His Ile Gly Gly Ser Pro Phe Lys	PRT
690 695 700 <213>	Homo saplens
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705 710 715 720 <221>	<221> human alpha enclase
Thr Ser Ser Val Phe Val Asp Ser Leu Thr Lys Ala Thr Cys Ala Pro	(1)(433)
725 730 735 <223>	Accession No. as of 29 August 2003; P06733
Gln His Gly Ala Pro Gly Pro Gly Pro Ala Asp Ala Ser Lys Val	61
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755 760 765	5
Phe Thr Val Asp Cys Ser Lys Ala Gly Asn Asn Met Leu Leu Val Gly	Pro Thr Val Glu Val Asp Leu Phe Thr Ser Lys Gly Leu Phe Arg Ala
770 775 780	20 25 30

WO 2004/053519 185/335 Ala Val Pro Ser Gly Ala Ser Thr Gly Ile Tyr Glu Ala Leu Glu Leu 35 Arg Asp Asp Asp Lys Thr Arg Tyr Met Gly Lys Gly Val Ser Lys Ala	PCT/EP1003/014057 T Glu Ala Leu Glu Leu 45 19 Gly Val Ser Lys Ala	WO 2004/055519 186/335 186/335 Leu Leu Lys Thr Ala Ile Gly Lys Ala Gly Tyr Thr Asp Lys Val Val 225 225 216 Gly Met Asp Val Ala Ala Ser Glu Phe Phe Arg Ser Gly Lys Tyr
50 55 60 Vel Glu His Ile Asn Lys Thr Ile Ala Pro Ala Leu Val 65	Ser Lys	245 Lys Ser Pro Asp
Leu Asn Val Thr Glu Glu Lys Ile Asp Lys Leu Met 85 90 Asp Gly Thr Glu Asn Lys Ser Lys Phe Gly Ala Asn Ala 100	80 s Leu Met Ile Glu Met 95 a Asn Ala Ile Leu Gly	250 270 Asp Gln Leu Ala Asp Leu Tyr Lys Ser Phe Ile Lys Asp Tyr Pro Val 275 280 285 Val Ser Ile Glu Asp Pro Phe Asp Gln Asp Asp Trp Gly Ala Trp Gln 10 290 295
Val Ser Leu Ala Val Cys Lys Ala Gly Ala Val Glu Lys Gly Val Pro 115 Leu Tyr Arg His Ile Ala Asp Leu Ala Gly Asn Ser Glu Val Ile Leu 130 135 140 Pro Val Pro Ala Phe Asn Val Ile Asn Gly Gly Ser His Ala Gly Asn	il Glu Lys Gly Val Pro 125 in Ser Glu Vel Ile Leu 140 y Ser His Ala Gly Asn	Val Val Gly Asp 315 Ala Val Asn Glu 330 .11e Gly Ser Val
145 Lys Leu Ala Met Gln Glu Phe Met Ile Leu Pro Val Gly 165 170 Phe Arg Glu Ala Met Arg Ile Gly Ala Glu Val Tyr His 180 180	155 160 Pro Val Gly Ala Ala Asn 175 Val Tyr His Asn Leu Lys 190	340 345 350 Leu Gln Ala Cys Lys Leu Ala Gln Ala Asn Gly Trp Gly Val Met Val 355 360 360 365 Ser His Arg Ser Gly Glu Thr Glu Asp Thr Phe Ile Ala Asp Leu Val 20 370 375 380
Asn Val Ile Lys Glu Lys Tyr Gly Lys Asp Ala Thr Asn 195 200 205 Glu Gly Gly Phe Ala Pro Asn Ile Leu Glu Asn Lys Glu 210 210	la Thr Asn Val Gly Asp 205 sn Lys Glu Gly Leu Glu	Val Gly Leu Cys Thr Gly Gln Ile Lys Thr Gly Ala Fro Cys Arg Ser 385 390 395 400 Glu Arg Leu Ala Lys Tyr Asn Gln Leu Leu Arg Ile Glu Glu Glu Leu 405 410 415

WO 2004/055519	187/335	PCT/EP2003/014057	WO 2004/055519 188/335	PCT/EP2003/014057
Gly Ser Lys Ala Lys Phe	Gly Ser Lys Ala Lys Phe Ala Gly Arg Asn Phe Arg Asn	sn Pro Leu Ala	01y Asn Pro Ala Pro Thr Ser Asn His Gly Pro Asp Ala Thr Glu Ala	Thr Glu Ala
420	425	430		80
Lys			Glu Glu Asp Phe Val Asp Pro Trp Thr Val Gln Thr Ser Ser Ala Lys	Ser Ala Lys
			95	. 56
S			5 Gly ile Asp Tyr Asp Lys Leu ile Val Arg Phe Gly Ser Ser Lys ile	Ser Lys Ile
			100 105	110
<210> 62			Asp Lys Glu Leu Ile Asn Arg Ile Glu Arg Ala Thr Gly Gln Arg Pro	Gln Arg Pro
<211> 471			115 . 120 125	
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10 <213> Homo sapiens			10 130 135 140	-
<2220>			Gln Val Leu Asp Ala Tyr Glu Asn Lys Lys Pro Phe Tyr Leu Tyr Thr	Leu Tyr Thr
<221> tryptophanyl-tRNA synthetase	synthetase		145 150 155	160
<222> (1)(471)			Gly Arg Gly Pro Ser Glu Ala Met His Val Gly His Leu Ile Pro	Leu Ile Pro
<223> Accession No. as	Accession No. as of 29 August 2003; P23381		165 170	175
15 <400> 62			15 Phe Ile Phe Thr Lys Trg Leu Gln Asp Val Phe Asn Val Pro Leu Val	Pro Leu Val
			180 185	190
Met Pro Asn Ser Glu Pro	Met Pro Asn Ser Glu Pro Ala Ser Leu Leu Glu Leu Phe	he Asn Ser Ile	ile Gin Met Thr Asp Asp Glu Lys Tyr Leu Trp Lys Asp Leu Thr Leu	Leu Thr Leu
1 8	10	15	195 200 205	
Ala Thr Gln Gly Glu Leu	Ala Thr Gln Gly Glu Leu Val Arg Ser Leu Lys Ala Gly	ly Asn Ala Ser	Asp Gln Ala Tyr Ser Tyr Ala Val Glu Asn Ala Lys Asp Ile Ile Ala	rie rie Ala
20 20	25	30	20 210 215 220	
Lys Asp Glu Ile Asp Ser	Lys Asp Glu Ile Asp Ser Ala Val Lys Met Leu Val Ser	er Leu Lys Met	Cys Gly Phe Asp Ile Asn iys Thr Phe Ile Phe Ser Asp Leu Asp Tyr	Leu Asp Tyr
35	40 45	vo	225 230 235	240
Ser Tyr Lys Ala Ala Ala	Ser Tyr Lys Ala Ala Ala Gly Glu Asp Tyr Lys Ala Asp	sp Cys Pro Pro	Met Gly Met Ser Ser Gly Phe Tyr Lys Asn Val Val Lys Ile Gln Lys	ile Gln Lys
50 .	. 25		245 250	255

	WO 2004/055519 PCT/EP2003/014057 189/335	WO 2004/055519 PCT/EP2003/014057 190/335
	His Val Thr Phe Asn Gln Val Lys Gly Ile Phe Gly Phe Thr Asp Ser	Arg Lys Glu Val Thr Asp Glu Ile Val Lys Glu Phe Met Thr Pro Arg
	. 260 265 270	450 455 460
	Asp Cys Ile Gly Lys Ile Ser Phe Pro Ala Ile Gln Ala Ala Pro Ser	Lys Leu Ser Phe Amp Phe Gln
	. 275 280 285	465 470
-	5 Phe Ser Asn Ser Phe Pro Gln Ile Phe Arg Asp Arg Thr Asp Ile Gln	
	290 295 300	
	Cys Leu Ile Pro Cys Ala Ile Asp Gln Asp Pro Tyr Phe Arg Met Thr	<210> 63
	305 310 315 320	<211> 106
	Arg Asp Val Ala Pro Arg Ile Gly Tyr Pro Lys Pro Ala Leu Leu His	<212> PRT
	10 325 330 335	10 <213> Homo sapiens
	Ser Thr Phe Pro Ala Leu Gln Gly Ala Gln Thr Lys Met Ser Ala	<220>.
	340 345 350 .	<221> Ig kappa chain C regionI
	Ser Asp Pro Asn Ser Ser Ile Phe Leu Thr Asp Thr Ala Lys Gln Ile	<222> (1)(106)
	355 360 365	<223> Accession No. as of 29 August 2003; P01834
	15. Lys Thr Lys Val Asn Lys His Ala Phe Ser Gly Gly Arg Asp Thr Ile	15 <400> 63
	370 375 380	
	Glu Glu His Arg Gln Phe Gly Gly Asn Cys Asp Val Asp Val Ser Phe	Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
	385 390 395 400	1 5 10 15
	Met Tyr Leu Thr Phe Phe Leu Glu Asp Asp Asp Lys Leu Glu Gln \cdot Ile	Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
	20 405 410 415	20 20 25 30
	Arg Lys Asp Tyr Thr Ser Gly Ala Met Leu Thr Gly Glu Leu Lys Lys	Pro Arg Glu Ala Lys Val Gin Trp Lys Val Asp Asn Ala Leu Gin Ser
	420 425 430	35 40 45
	Ala Leu Ile Glu Val Leu Gln Pro Leu Ile Ala Glu His Gln Ala Arg	Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
÷	435 440 445	09 55 05
. * .		

WO 2004/055519 PCT/EP2003/014057 191/335	WO 2004/055519 PCT/EP2003/014057 192/335
Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys	Ala Gly Leu Leu Phe Val Gly Gly Gly Gly Thr Ile Leu Tyr
65 70 75 80	
His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro	Ala Lys Trp Asp Ser His Phe Arg Glu Ser Val Glu Lys Thr Ile Pro
85 90 95	. 65 70 75 80
5 Val Thr Lys Ser Phe Asn Arg Gly Glu Cys	5 Tyr Ser Asp Lys Leu Phe Glu Met Val Leu Gly Pro Ala Ala Tyr Asn
100 105	96 90 98
	Val Pro Leu Pro Lys Lys Ser Ile Gln Ser Gly Pro Leu Lys Ile Ser
	100 105 110
<210> 64	Ser Val Ser Glu Val Met Lys Glu Ser Lys Gln Pro Ala Ser Gln Leu
10 <211> 758	10 115 120 125
<212> PRT	Gln Lys Gln Lys Gly Asp Thr Pro Ala Ser Ala Thr Ala Pro Thr Glu
<213> Homo sapiens	130 135 140
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<221> Mitofilin	145 150 155 160
15 <222> (1)(758)	15 Pro Ala Val Gin Pro Glu Glu Ser Leu Lys Thr Asp His Pro Glu Ile
<223> Accession No. as of 29 August 2003; Q16891	165 170 175
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	180 185 190
Met Leu Arg Ala Cys Gln Leu Ser Gly Val Thr Ala Ala Ala Gln Ser	Ser Ile Arg Glu Arg Pro Pro Glu Glu Val Ala Ala Arg Leu Ala Gln
20 1 5 10 15	20 1.95 2.00. 2.05
Cys Leu Cys Gly Lys Phe Val Leu Arg Pro Leu Arg Pro Cys Arg Arg	Gin Glu Lys Gin Glu Gin Val Lys Ile Glu Ser Leu Ala Lys Ser Leu
20 25 30	210 215 220
Tyr Ser Thr Ser Gly Ser Gly Leu Thr Thr Gly Lys Ile Ala Gly	Glu Asp Ala Leu Arg Gln Thr Ala Ser Val Thr Leu Gln Ala Ile Ala
35 40 45	225 230 235 240

WO 2004/055519 PCT/EP2003/014057	Ale Leu Glu Lys Gln Lys Leu Glu Glu Lys Arg Ala Phe Asp Ser Ala	435 440 445	Val Ala Lys Ala Leu Glu His His Arg Ser Glu Ile Gln Ala Glu Gln	450 455 460	5 Asp Arg Lys Ile Glu Glu Val Arg Asp Ala Met Glu Asn Glu Met Arg	465 470 475 480	Thr Gln Leu Arg Arg Gln Ala Ala His Thr Asp His Leu Arg Asp	485 490 495	Val Leu Arg Val Gin Giu Giu Leu Lys Ser Giu Phe Giu Gin Asn	10 500 505 510	Leu Ser Glu Lys Leu Ser Glu Gln Glu Leu Gln Phe Arg Arg Leu Ser	515 520 525	Gin Giu Gin Val Asp Asn Phe Thr Leu Asp Ile Asn Thr Ala Tyr Ala	530 535 540	15 Arg Leu Arg Gly Ile Glu Gln Ala Val Gln Ser His Ala Val Ala Glu	545 550 555 560	Glu Glu Ala Arg Lys Ala His Gln Leu Trp Leu Ser Val Glu Ala Leu	565 570 575	Lys Tyr Ser Met Lys Thr Ser Ser Ala Glu Thr Pro Thr Ile Pro Leu	20 580 585 590	Gly Ser Ala Val Glu Ala Ile Lys Ala Asn Cys Ser Asp Asn Glu Phe	509	
WO 2004/055519 PCT/EP2003/014057	Ala Gin Asn Ala Ala Val Gin Ala Val Asn Ala His Ser Asn Ile Leu	245 250 255	Lys ala Ala Met Asp Asn Ser Glu Ile Ala Gly Glu Lys Lys Ser Ala	260 265 270	Gin Trp Arg Thr Val Glu Gly Ala Leu Lys Glu Arg Arg Lys Ala Val	275 280 285	Asp Glu Ala Ala Asp Ala Leu Leu Lys Ala Lys Glu Glu Leu Glu Lys	290 295 300	Met Lys Ser Val 11e Glu Asn Ala Lys Lys Lys Glu Val Ala Gly Ala	305 310 315 320	Lys Pro His Ile Thr Ala Ala Glu Gly Lys Leu His Asn Met Ile Val	325 330 335	Asp Leu Asp Asn Val Val Lys Lys Val Gln Ala Ala Gln Ser Glu Ala	340 345 350	Lys Val Val Ser Gln Tyr His Glu Leu Val Val Gln Ala Arg Asp Asp	355 360 365	Phe Lys Arg Glu Leu Asp Ser Ile Thr Pro Glu Val Leu Pro Gly Trp	370 375 380	Lys Gly Met Ser Val Ser Asp Leu Ala Asp Lys Leu Ser Thr Asp Asp	20 385 390 395 400	Leu Asn Ser Leu Ile Ala His Ala His Arg Arg Ile Asp Gln Leu Asn	405 410 415	

WO 2004/055519 PCT/RP2003/014057 196/335	<220 >	<221> Ribisoms-binding protein 1	<222> (1)(1410)	<223> Accession No. as of 29 August 2003: 075300	5 <400> 65		Met Asp Ile Tyr Asp Thr Gln Thr Leu Gly Val Val Val Phe Gly Gly	1 5 10 15	Phe Met Val Val Ser Ala Ile Gly Ile Phe Leu Val Ser Thr Phe Ser	10 20 25 .30	Met Lys Glu Thr Ser Tyr Glu Glu Ala Leu Ala Asn Gln Arg Lys Glu	35 40 45	Met Ala Lys Thr His His Gln Lys Val Glu Lys Lys Lys Lys Glu Lys	. 09 55 05	15 Thr Val Glu Lys Lys Gly Lys Thr Lys Lys Lys Glu Glu Lys Pro Asn	65 70 75 80	Gly Lys Ile Pro Asp His Asp Pro Ala Pro Asn Val Thr Val Leu	56 06 58	Arg Glu Pro Val Arg Ala Pro Ala Val Ala Val Ala Pro Thr Pro Val	20 100 105 110	Gin Pro Pro ile ile Val Ala Pro Val Ala Thr Vel Pro Ala Met Pro	115 120 125	Gin Giu Lys Leu Ala Ser Ser Pro Lys Asp Lys Lys Lys Lys Giu Lys	130 135 140		
WO 2004/055519 PCT/EP2003/014057 195/335	Val Tyr Ser Glu Glu Thr Leu Arg Ala Arg Phe Tyr Ala Val Gln Lys	625 630 635 640	Leu Ala Arg Arg Val Ala Met Ile Asp Glu Thr Arg Asn Ser Leu Tyr	645 650 655	5 Gln Tyr Phe Leu Ser Tyr Leu Gln Ser Leu Leu Leu Phe Pro Pro Gln	660 665 670	Gln Leu Lys Pro Pro Glu Leu Cys Pro Glu Asp 11e Asn Thr Phe	675 680 685	Lys Leu Leu Ser Tyr Ala Ser Tyr Cys Ile Glu His Gly Asp Leu Glu	10 690 695 700	Leu Ala Ala Lys Phe-Val Asn Gln Leu Lys Gly Glu Ser Arg Arg Val	705 710 715 720	Ala Gin Asp Trp Leu Lys Glu Ala Arg Met Thr Leu Glu Thr Lys Gln	725 730 735	15 Ile Val Glu Ile Leu Thr Ala Tyr Ala Ser Ala Val Gly Ile Gly Thr	740 745 750	Thr Gln Val Gln Pro Glu	755		20	<210> 65	<211> 1410	<212> PRT	<213> Homo sapiens		

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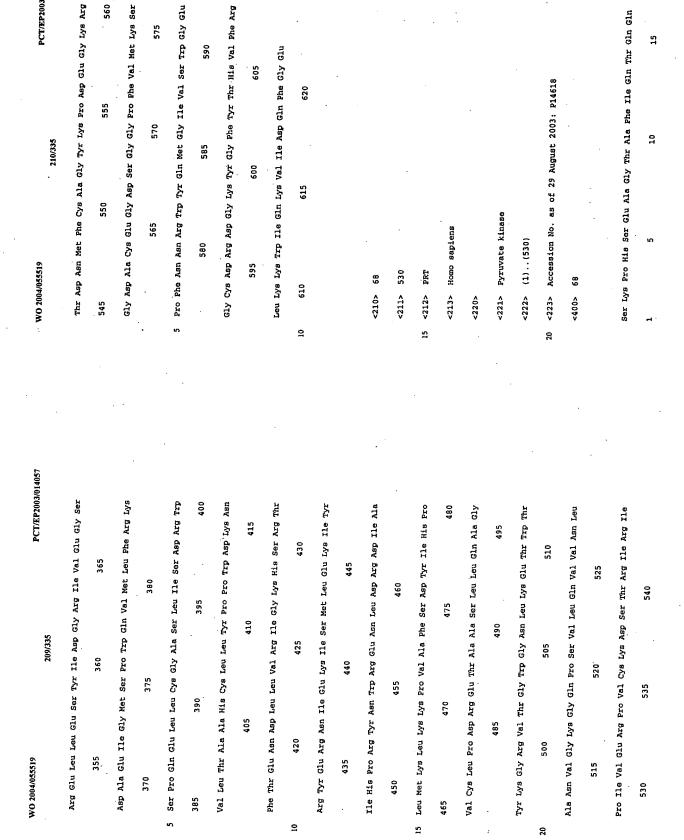
	WO 2004/055519		PCT/EP2003/014057	· WO 2004/055519	PCT/EP2003/014057
		199/335		. 200/335	
	Lys Ala Glu Arg Ser P	Lys Ala Glu Arg Ser Pro Asn Gln Gly Lys Lys Gly Glu Gly Ala	Gly Ala Pro	Ser Lys Leu Arg Glu Leu Agn Lys Glu Met Ala Ala Glu Lys Ala Lys	Lys Ala Lys
	530	535 540		725 730	735
	ile Gin Gly Lys Lys A	ile Gin Gly Lys Lys Ala Asp Ser Val Ala Asn Gin Gly T	Thr Lys Val	Ala Ala Ala Gly Glu Ala Lye Val Lye Lye Gln Leu Val Ala Arg Glu	Ala Arg Glu
	545 5:	550 555		740 745	750
Ŋ	Glu Gly Ile Thr Asn G	Glu Gly Ile Thr Asn Gln Gly Lys Lys Ala Glu Gly Ser P	Pro Ser Glu	5 Gin Glu Ile Thr Ala Val Gin Ala Arg Met Gin Ala Ser Tyr Arg Glu	Tyr Arg Glu
	565	570	575	. 755 760 765	
•	Gly Lys Lys Ala Glu G	Gly Lys Lys Ala Glu Gly Ser Pro Asn Gln Gly Lys Lys Ala Asp Ala	Ala Asp Ala	His Val Lys Glu Val Gln Gln Leu Gln Gly Lys Ile Arg Thr Leu Gln	Thr Leu Gln
	280	585	290	770 775 780	
	Ala Ala Asn Gln Gly L	Ala Ala Asn Gln Gly Lys Lys Thr Glu Ser Ala Ser Val Gln Gly Arg	Gln Çly Arg	Glu Glu Leu Glu Asn Gly Pro Asn Thr Gln Leu Ale Arg Leu Gln Gln	Leu Gln Gln
01	595	909	:	10 785 790 795	800
	Asn Thr Asp Val Ala G	Asn Thr Asp Val Ala Gln Ser Pro Glu Ala Pro Lys Gln Glu Ala Pro	Glu Ala Pro	Glu Asn Ser Ile Leu Arg Asp Ala Leu Asn Gln Ala Thr Ser Gln Val	Ser Gln Val
	610	615 620		. 810	
	Ala Lys Lys Lys Ser G	Ala Lys Lys Lys Ser Gly Ser Lys Lys Lys Gly Glu Pro Gly Pro Pro	Gly Pro Pro	Glu Ser Lys Gln Asn Ala Glu Leu Ala Lys Leu Arg Gln Glu Leu Ser	Glu Leu Ser
	625 6.	630 635	640	825	. 028
15	Asp Ala Asp Gly Pro L	Asp Ala Asp Gly Pro Leu Tyr Leu Pro Tyr Lys Thr Leu V	al Ser Thr	15 Lys Val Ser Lys Glu Leu Val Glu Lys Ser Glu Ala Val Arg Gln Asp	Arg Gln Asp
	. 645	059	655	835 840 845	•
	Val Gly Ser Met Val P	Val Gly Ser Met Val Phe Asn Glu Gly Glu Ala Gln Arg Leu Ile Glu	fleu ile Glu	Glu Gln Gln Arg Lys Ala Leu Glu Ala Lys Ala Ala Ala Phe Glu Lys	Phe Glu Lys
	999	665	670	098 558 058	
	ile Leu Ser Glu Lys A	ile Leu Ser Glu Lys Ala Gly Ile Ile Gln Asp Thr Trp His Lys) His Lys Ala	Gin Val Leu Gin Leu Gin Ala Ser His Arg Glu Ser Glu Glu Ala Leu	Glu Ala Leu
20	675	680 685		20 865 870 875	880
	Thr Gln Lys Gly Asp P	Thr Gln Lys Gly Asp Pro Val Ala Ile Leu Lys Arg Gln Leu Glu Glu	ı Leu Glu Glu	Gin Lys Arg Leu Asp Glu Val Ser Arg Glu Leu Cys His Thr Gin Ser	Thr Gln Ser
	069	700		885. 890	895
	Lys Glu Lys Leu Lau A	Lys Glu Lys Leu Leu Ala Thr Glu Gln Glu Asp Ala Ala	Val Ala Lys	Ser His Ala Ser Leu Arg Ala Asp Ala Glu Lys Ala Gln Glu Gln Gln	Glu Gln Gln
	705	710 715	720	506 006	910

	WO 2004/055519	PCT/EP2003/014057 201/335		WO 2004/055519		202/335	PCT/EP2003/01
	Gln Gln Met Ala Glu	Gin Gin Met Ala Giu Leu His Ser Lys Leu Gin Ser Ser Giu Ala Giu		His Pro	Pro Ala Pro Ala Glu Pro Ser Ser Asp Leu	Ser Ser Asp Leu	Ala Ser Lys
	915	920 925		1100	1105	1110	
	Val Arg Ser Lys Cys	Val Arg Ser Lys Cys Glu Glu Leu Ser Gly Leu His Gly Gln Leu Gln		Leu Arg	Glu Ala Glu Glu Thr	Gln Ser Thr Leu Gln	Ala Glu Cys
	026	935 940		1115	1120	1125	
'n	Glu Ala Arg Ala Glu	Glu Ala Arg Ala Glu Asn Ser Gln Leu Thr Glu Arg Ile Arg Ser Ile	•	5 Asp Gln	Tyr Arg Ser Ile Leu	Ala Glu Thr Glu Gly	Met Leu Arg
	945	096 . 056		1130	30 1135	1140	
	Glu Ala Leu Leu Glu	Glu Ala Leu Leu Glu Ala Gly Gln Ala Arg Asp Ala Gln Asp Val Gln	-	Asp Leu	Gln Lys Ser Val Glu	Glu Glu Glu Glu Val	Trp Arg Ala
	965	970 975		1145	1150	1155	
	Ala Ser Gln Ala Glu	Ala Ser Gln Ala Glu Ala Asp Gln Gln Gln Thr Arg Leu Lys Glu Leu		Lys Val	l Gly Ala Ala Glu Glu Leu Gln Lys Ser		Arg Val Thr
2	086	066 586 .		1160	50 1165	11,70	
•	Glu Ser Gln Val Ser (Glu Ser Gln Val Ser Gly Leu Glu Lys Glu Ala Ile Glu Leu Arg Glu		Val Lys	His Leu Glu Glu Ile Val Glu Lys Leu Lys		Gly Glu Leu
	995	1000		1175	1180	1185	
	Ala Val Glu Gln Gln	Glu Gln Gys Val Lys Asn Asn Asp Leu Arg Glu Lys		Glu Ser	Ser Asp Gln Val Arg	Glu His Thr Ser His	Leu Glu Ala
	1010	1015 1020		1190	90 1195	1200	
15	Asn Trp Lys Ala Met	Lys Ala Met Glu Ala Leu Ala Thr Ala Glu Gln Ala Cys		15 Glu Leu	. Glu Lys His Met Ala Ala Ala Ser Ala Glu		Cys Gln Asn
	1025	1030 1035		12	1205 1210	1215	
	Lys Glu Lys Leu Leu	Lys Leu Leu Ser Leu Thr Gln Ala Lys Glu Glu Ser Glu		Tyr Ala	a Lys Glu Val Ala Gly Leu Arg Gln Leu Leu	a Arg Gln Leu Leu	Leu Glu Ser
	1040	1045 1050		1220	20 1225	1230	
	Lys Gln Leu Cys Leu	Leu Cys Leu Ile Glu Ala Gln Thr Met Glu Ala Leu Leu		Gln Ser	r Gin Leu Asp Ala Ala Lys Ser Glu Ala Gin	s Ser Glu Ala Gin	Lys Gln Ser
20	1055	1060 1065		20 12	1235 1240	1245	
	Ala Leu Leu Pro Glu	Ala Leu Leu Pro Glu Leu Ser Val Leu Ala Gln Gln Asn Tyr Thr		Asp Gl	Asp Glu Leu Ala Leu Val Arg Glr	Gln Gln Leu Ser Glu	Met Lys Ser
	1070	1075 1080		12	1250 1255	1260	
	Glu Trp Leu Gln Asp	Glu Trp Leu Gln Asp Leu Lys Glu Lys Gly Pro Thr Leu Leu Lys		His Val	l Glu Asp Gly Asp Ile Ala Gly Ala Pro Ala		Ser Ser Pro
	1085	1090 1095		1265	1270	1275	

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WO 2004/055519 Gln Lys Ile	/O 2004/055519 205/335 Gln Lys Ile Val Asn Leu Lys Glu Lys Val Ala Gln I 145 155	205/335 Slu Lys Val Ala Gln 155	PCT/EP2003/014057 Leu Glu Ala Gln 160		WO 2004/055519 206/335 Gin Phe Ser Thr Trp Asp Asn Asp Asn Asp Lys Phe Glu Gly Asn Cys 340 345	PCT/EP2003/014057 335 an Asp Lys Phe Glu Gly Asn Cys 350	
Cys Gln (Cys Gin Giu Pro Cys Lys Asp Thr Val Gin 11e His Asp 11e Thr Gly 176	thr Val Gln lle His. 170	Asp Ile Thr Gly 175		Ala Glu Gln Asp Gly Ser Gly Trp Trp Met Asn Lys Cys His Ala Gly	rp Met Asn Lys Cys His Ala Gly 365	
5 гуз Азр С	Lys Asp Cys Gln Asp Ile Ala Asn Lys Gly Ala Lys Gln Ser Gly Leu 180	ksn Lys Gly Ala Lys (185	Gln Ser Gly Leu 190	v n .	His Leu Asn Gly Val Tyr Gln Gly Gly Thr Tyr Ser Lys Ala Ser 370 375 380	ly Gly Thr Tyr Ser Lys Ala Ser 380	
Tyr Phe 1	Tyr Phe 11e Lys Pro Leu Lys Ala Asn Gln Gln Phe Leu Val Tyr 195 200	Ala Asn Gin Gin Phe 1 200	Leu Val Tyr Cys 205		Thr Pro Asn Gly Tyr Asp Asn Gly Ile Ile Trp Ala Thr Trp Lys Thr 385 395 400	e lle Trp Ala Thr Trp Lys Thr 395 400	
Glu Ile.A	Glu Ile Asp Gly Ser Gly Asn Gly Trp Thr Val Phe Gln Lys Arg Leu 210	sly Trp Thr Val Phe (Gln Lys Arg Leu	01	Arg Trp Tyr Ser Met Lys Lys Thr Thr Met Lys Ile Ile Pro Phe Asn 405 410 415	r Met Lys Ile Ile Pro Phe Asn 410 410	
Asp Gly S 225	Asp Gly Ser Val Asp Phe Lys Lys Asn Trp Ile Gln Tyr Lys Glu Gly 225 235 230 240	у9 Asn Trp Ile Gln : , 235	Tyr Lys Glu Gly 240		Arg Leu Thr Ile Gly Glu Gly Gln Gln His His Leu Gly Gly Ala Lys	n His His Leu Gly Gly Ala Lys	
Phe Gly F	Phe Gly His Leu Ser Pro Thr Gly Thr Thr Glu Phe Trp Leu Gly Asn 245	ily Thr Thr Glu Phe ? 250	Trp Leu Gly Asn 255		Gln Val Arg Pro Glu His Pro Ala Glu Thr Glu Tyr Asp Ser Leu Tyr 435 440	u Thr Glu Tyr Asp Ser Leu Tyr 445	
15 Glu Lys I	Glu Lys lle His Leu Ile Ser Thr Gln Ser Ala Ile Pro Tyr Ala Leu 260 265 270	hr Gln Ser Ala Ile 1 265	Pro Tyr Ala Leu 270	15	Pro Glu Asp Asp Leu 450		
7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	275	280 111 Set 712 280 280 280 280 280 280 280 280 280 28	inz Ala Asp iyz 285				
Ala Met P 20 290	Ala Met Phe Lys Val Gly Pro Glu Ala Asp Lys Tyr Arg Leu Thr Tyr 290	ilu Ala Asp Lys Tyr ? 300	Arg Leu Thr Tyr	20	<210> 67 <211> 622		
Ala Tyr P 305	Ala Tyr Phe Ala Gly Gly Asp Ala Gly Asp Ala Phe Asp 310 316 316	la Gly Asp Ala Phe <i>1</i> 315	Авр Gly Phe Asp 320		<212> PRT <213> Homo sepiens		•
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w	WO 2004/055519 207/335	PCT/EP2003/014057	WO 2004/055519	PCT/EP2003/014057
2	<222> (1)(622)		Asp Ser Ser Thr Thr Gly	Asp Ser Ser Thr Thr Gly Pro Trp Cys Tyr Thr Thr Asp Pro Thr Val
\$	<223> Accession No. as of 29 August 2003; P00734	P00734	165	170 175
Ÿ	<400> 67		Arg Arg Gln Glu Cys Ser	Arg Arg Gin Glu Cys Ser Ile Pro Val Cys Gly Gin Asp Gln Val Thr
			180	185 190
5 Me	Met Ala His Val Arg Gly Leu Gln Leu Pro Gly Cys Leu Ala Leu Ala	' Cys Leu Ala Leu Ala	5 Val Ala Met Thr Pro Arg	Val Ala Met Thr Pro Arg Ser Glu Gly Ser Ser Val Asn Leu Ser Pro
н	5 10	15	195	200 . 205
A.	Ala Leu Cys Ser Leu Val His Ser Gln His Val Phe Leu Ala Pro	. Phe Leu Ala Pro Gln	Pro Leu Glu Gln Cys Val	Pro Leu Glu Gln Cys Val Pro Asp Arg Gly Gln Gln Tyr Gln Gly Arg
	20 25	30	210	215 220
ច	Gln Ala Arg Ser Leu Leu Gln Arg Val Arg Arg Ala Asn T	Ala Asn Thr Phe Leu	Leu Ala Val Thr Thr His	Leu Ala Val Thr Thr His Gly Leu Pro Cys Leu Ala Trp Ala Ser Ala
10	35 40	45	10 225 230	235 240
ច	Glu Glu Val Arg Lys Gly Asn Leu Glu Arg Glu Cys Val	. Cys Val Glu Glu Thr	Gln Ala Lys Ala Leu Ser	Ghn Ala Lys Ala Leu Ser Lys His Gin Asp Phe Asn Ser Ala Val Gin
	50 55	09	245	250 255
Š	Cys Ser Tyr Glu Glu Ala Phe Glu Ala Leu Glu Ser Ser Thr Ala Thr	Ser Ser Thr Ala Thr	Leu Val Glu Asn Phe Cys	Leu Val Glu Asn Phe Cys Arg Asn Pro Asp Gly Asp Glu Glu Gly Val
65	57 . 07 75	08	. 260	265 . 270
15 As	Asp Val Phe Trp Ala Lys Tyr Thr Ala Cys Glu Thr Ala Arg Thr Pro	Thr Ala Arg Thr Pro	15 Trp Cys Tyr Val Ala Gly	Trp Cys Tyr Val Ala Gly Lys Pro Gly Asp Phe Gly Tyr Cys Asp Leu
	85 90	95	275	280 285
¥	Arg Asp Lys Leu Ala Ala Cys Leu Glu Gly Asn Cys Ala Glu Gly Leu	. Cys Ala Glu Gly Leu	Asn Tyr Cys Glu Glu Ala	Asn Tyr Cys Glu Glu Ala Val Glu Glu Glu Thr Gly Asp Gly Leu Asp
	100 105	110	290	300
ច	Gly Thr Asn Tyr Arg Gly His Val Asn Ile Thr Arg Ser Gly Ile Glu	Arg Ser Gly Ile Glu	Glu Asp Ser Asp Arg Ala	Glu Asp Ser Asp Arg Ala Ile Glu Gly Arg Thr Ale Thr Ser Glu Tyr
20	. 115 120	125	20 305 310	315 320
ζ	Cys Gln Leu Trp Arg Ser Arg Tyr Pro His Lys Pro Glu Ile	Pro Glu Ile Asn Ser	Gln Thr Phe Phe Asn Pro	Gin Thr Phe Phe Asn Pro Arg Thr Phe Gly Ser Gly Glu Ale Asp Cys
	130 135	140	325	330 335
뜌	Thr Thr His Pro Gly Ala Asp Leu Gln Glu Asn Phe Cys Arg Asn Pro	Phe Cys Arg Asn Pro	Gly Leu Arg Pro Leu Phe	Gly Leu Arg Pro Leu Phe Glu Lys Lys Ser Leu Glu Asp Lys Thr Glu
1.45	150 155	160	340	345 350
				•



a ,			,
	WO 2004/055519 PCT/EP2003/014057 211/335	WO 2004/055519 PCT/EP2003/014057 212/335	
	Leu His Ala Ala Met Ala Asp Thr Phe Leu Glu His Met Cys Arg Leu	Asn Leu Pro Gly Ala Ala Val Asp Leu Pro Ala Val Ser Glu Lys Asp	
	20. 25 30	210 215 220	
	Asp ile Asp Ser Pro Pro ile Thr Ala Arg Asn Thr Gly ile ile Cys	Ile Gln Asp Leu Lys Phe Gly Val Glu Gln Asp Val Asp Met Val Phe	
	35 40 45	225 230 235 240	
	5 Thr lle Gly Pro Ala Ser Arg Ser Val Glu Thr Leu Ly8 Glu Met Ile	5 Ala Ser Phe Ile Arg Lys Ala Ser Asp Vel His Glu Vel Arg Lys Val	
	09 55 09	245 250 255	
•	Lys Ser Gly Met Asn Val Ala Arg Leu Asn Phe Ser His Gly Thr His	Leu Gly Glu Lys Gly Lys Asn Ile Lys Ile Ile Ser Lys Ile Glu Asn	
	65 70 75 80	260 265 270	
	Glu Tyr His Ala Glu Thr Ile Lys Asn Val Arg Thr Ala Thr Glu Ser	His Glu Gly Val Arg Arg Phe Asp Glu Ile Leu Glu Ala Ser Asp Gly	
-	10 85 90 95	10 275 280 285	
	Phe Ala Ser Asp Pro Ile Leu Tyr Arg Pro Val Ala Val Ala Leu Asp	Ile Met Val Ala Arg Gly Asp Leu Gly Ile Glu Ile Pro Ala Glu Lys	
	100 105 110	290 295 300	
	Thr Lys Gly Pro Glu Ile Arg Thr Gly Leu Ile Lys Gly Ser Gly Thr	Val Phe Leu Ala Gln Lys Met Met Ile Gly Arg Cys Asn Arg Ala Gly	
. '	115 120 125	305 310 315 320	
	15 Ala Glu Val Glu Leu Lys Lys Gly Ala Thr Leu Lys Ile Thr Leu Asp	15 Lys Pro Val Ile Cys Ala Thr Gln Met Leu Glu Ser Met Ile Lys Lys	
•	130 . 135 140	325 330 335	
	Asn Ala Tyr Met Glu Lys Cys Asp Glu Asn Ile Leu Trp Leu Asp Tyr	Pro Arg Pro Thr Arg Ala Glu Gly Ser Asp Val Ala Asn Ala Val Leu	
	145 150 155 160	340 345 350	
	Lys Asn lle Cys Lys Val Val Glu Val Gly Ser Lys Ile Tyr Val Asp	Asp Gly Ala Asp Cys Ile Met Leu Ser Gly Glu Thr Ala Lys Gly Asp	
	20 165 170 175	20 355 360 365	
	Asp Gly Leu lle Ser Leu Gln Val Lys Gln Lys Gly Ala Asp Phe Leu	Tyr Pro Leu Glu Ala Val Arg Met Gln His Leu Ile Ala Arg Glu Ala	
	180 185 190	370 375 380	
	Val Thr Glu Val Glu Asn Gly Gly Ser Leu Gly Ser Lys Lys Gly Val	Glu Ala Ala Ile Tyr His Leu Gln Leu Phe Glu Glu Leu Arg Arg Leu	
	200 205	385 390 395 400	
•			

WO 2004/055519 213/335 213/335	WO 2004/055519 PCT/EP2003/014057	1057
Ala Pro Ile Thr Ser Asp Pro Thr Glu Ala Thr Ala Val Gly Ala Val	<220>	
405 410 415	<221> Reticulocalbin 3 precursor	
Glu Ala Ser Phe Lys Cys Cys Ser Gly Ala Ile Ile Val Leu Thr Lys	<222> (1)(328)	
420 425 430	<223> Accession No. as of 29 August 2003: Q96D15	
5 Ser Gly Arg Ser Ala His Gln Vel Ale Arg Tyr Arg Pro Arg Ala Pro	5 <400> 69	
435 440 445		
Ile Ile Ala Val Thr Arg Asn Pro Gln Thr Ala Arg Gln Ala His Leu	Met Met Trp Arg Pro Ser Val Leu Leu Leu Leu Leu Leu Leu Arg His	
450 455 460	1. 5 7 10 . 15	
Tyr Arg Gly ile Phe Pro Val Leu Cys Lys Asp Pro Val Gln Glu Ala	Gly Ala Gin Gly Lys Pro Ser Pro Asp Ala Gly Pro His Gly Gln Gly	
10 465 470 475 , 480	10 20 25 30	
Trp Ala Glu Asp Val Asp Leu Arg Val Asn Phe Ala Met Asn Val Gly	Arg Val His Gin Ala Ala Pro Leu Ser Asp Ala Pro His Asp Asp Ala	
485 490 495	35 40 45	
Lys Ala Arg Gly Phe Lys Lys Gly Asp Val Val Ile Val Leu Thr	His Gly Asn Phe Gln Tyr Asp His Glu Ala Phe Leu Gly Arg Glu Val	
500 505 510	50 55 60	
15 Gly Trp Arg Pro Gly Ser Gly Phe Thr Asn Thr Met Arg Val Val Pro	15 Ala Lys Glu Phe Asp Gln Leu Thr Pro Glu Glu Ser Gln Ala Arg Leu	
515 . 520 525	65 70 75 80	
Val Pro	Gly Arg Ile Val Asp Arg Met Asp Arg Ala Gly Asp Gly Asp Gly Trp	
530	85 . 06 . 28	
	Val Ser Leu Ala Glu Leu Arg Ala Trp Ile Ala His Thr Gln Gln Arg	
20	20 100 105 110	
<210> 69	His Ile Arg Asp Ser Val Ser Ala Ala Trp Asp Thr Tyr Asp Thr Asp	
<211> 328	115 120 125	
<212> PRT	Arg Asp Gly Arg Val Gly Trp Glu Glu Leu Arg Asn Ala Thr Tyr Gly	
<213> Homo sapiens	130 135 140	

	WO 2004/055519	215/335	PCT/EP2003/014057		WO 2004/055519	PCT/EP2003/0
	His Tyr Ala Pro	His Tyr Ala Pro Gly Glu Glu Phe His Asp Val Glu A	Glu Asp Ala Glu Thr			
	145	150 155	160	-		
	Tyr Lys Lys Met	Tyr Lys Lys Met Leu Ala Arg Asp. Glu Arg Arg Phe Arg Val Ala Asp	Arg Val Ala Asp		<210> 70	
	•	165 170	175	,	<211> 469	
	5 Gln Asp Gly Asp 9	Gln Asp Gly Asp Ser Met Ala Thr Arg Glu Glu Leu Thr Ala Phe Leu	Thr Ala Phe Leu	- -	5 <212> PRT	
	180	185	190		<213> Homo sapiens	
	His Pro Glu Glu	His Pro Glu Glu Phe Pro His Met Arg Asp Ile Val I	al ile Ala Glu Thr		<2220>	
	195	200	205		<221> Desmin	
	Leu Glu Asp Leu	Leu Glu Asp Leu Asp Arg Asn Lys Asp Gly Tyr Val G	al Gln Val Glu Glu		<222> (1)(469)	
10	210	215 220		01	<223> Accession No. as of 29 August 2003: P17661	2003: P17661
	Tyr ile Ala Asp i	Tyr Ile Ala Asp Leu Tyr Ser Ala Glu Pro Gly Glu Glu Glu Pro Ala	lu Glu Pro Ala		<400> 70	
	225	230 . 235	240			
	Trp Val Gln Thr 6	Trp Val Gln Thr Glu Arg Gln Gln Phe Arg Asp Phe A	Phe Arg Asp Leu Asn	•	Ser Gin Ala Tyr Ser Ser Gin Arg Val Ser Ser Tyr Arg Arg Thr	æl Ser Ser Tyr Arg Arg Thr
	44	245 250	255		. 1	10 15
13		Lys Asp Gly His Leu Asp Gly Ser Glu Val Gly His T	is Trp Val Leu Pro	. ŠI	Phe Gly Gly Ala Pro Gly Phe Pro Leu Gly Ser Pro Leu Ser Ser Pro	31y Ser Pro Leu Ser Ser Pro
	260	265	270		20 25	30
	Pro Ala Gln Asp G	Pro Ala Gln Asp Gln Pro Leu Val Glu Ala Asn His Leu Leu His Glu	en Leu His Glu		Val Phe Pro Arg Ala Gly Phe Gly Ser Lys Gly Ser Ser Ser Ser Val	ys Gly Ser Ser Ser Val
	275	280 28	285		35	24 70
	Ser Asp Thr Asp L	Ser Asp Thr Asp Lys Asp Gly Arg Leu Ser Lys Ala Glu Ile Leu Gly	ilu Ile Leu Gly		Thr Ser Arg Val Tyr Gln Val Ser Arg Thr Ser Gly Gly Ala Gly Gly	hr Ser Gly Gly Ala Gly Gly
20	290	. 295 300		20		.09
	Asn Trp Asn Met P	Asn Trp Asn Met Phe Val Gly Ser Gin Ala Thr Asn Tyr Gly Glu Asp	yr Gly Glu Asp		Leu Gly Ser Leu Arg Ala Ser Arg Leu Gly Thr Thr Arg Thr Pro Ser	ily Thr Thr Arg Thr Pro Ser
	305	310 315	320		65 70	75 80
	Leu Thr Arg His His Asp Glu Leu	is Asp Glu Leu		٠	Ser Tyr Gly Ala Gly Glu Leu Leu Asp Phe Ser Leu Ala Asp Ala Val	he Ser Leu Ala Asp Ala Val
	ĸ	325			85 90	. 95

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WO 2004/055519 PCT/EP2003/014057 217/335	WO 2004/055519 PCT/EP2003/014057 218/335
Asn Gln Glu Phe Leu Thr Arg Thr Asn Glu Lys Val Glu Leu Gln	Ser Glu Ala Glu Glu Trp Tyr Lys Ser Lys Val Ser Asp Leu Thr Gln
100 105 110	290 295 300
Glu Leu Asn Asp Arg Phe Ala Asn Tyr Ile Glu Lys Val Arg Phe Leu	Ala Ala Asn Lys Asn Asn Asp Ala Leu Arg Gln Ala Lys Gln Glu Met
115 120 125	305 310 315 .320
5 Glu Gln Gln Asn Ala Ala Leu Ala Ala Glu Val Asn Arg Leu Lys Gly	5 Met Glu Tyr Arg His Gln Ile Gln Ser Tyr Thr Cys Glu Ile Asp Ala
130 135 140	325 330 335
Arg Glu Pro Thr Arg Val Ala Glu Leu Tyr Glu Glu Glu Leu Arg Glu	Leu Lys Gly Thr Asn Asp Ser Leu Met Arg Gln Met Arg Glu Leu Glu
145 150 155 160	340 345 350
Leu Arg Arg Gln Val Glu Val Leu Thr Asn Gln Arg Ala Arg Val Asp	Asp Arg Phe Ala Ser Glu Ala Ser Gly Tyr Gln Asp Asn Ile Ala Arg
10 165 170 175	10 355 360 365
Val Glu Arg Asp Asn Leu Leu Asp Asp Leu Gln Arg Leu Lys Ala Lys	Leu Glu Glu Glu Ile Arg His Leu Lys Asp Glu Met Ala Arg His Leu
180 185 190	370 375 360
Leu Gln Glu Glu Ile Gln Leu Lys Glu Glu Ala Glu Asn Asn Leu Ala	Arg Glu Tyr Gln Asp Leu Leu Asn Val Lys Met Ala Leu Asp Val Glu
200 205	385 390 395 400
15 Ala Phe Arg Ala Asp Val Asp Ala Ala Thr Leu Ala Arg Ile Asp Leu	15 Ile Ala Thr Tyr Arg Lys Leu Leu Glu Gly Glu Glu Ser Arg Ile Asn
210 215 220	405 410 415
Glu Arg Arg Ile Glu Ser Leu Asn Glu Glu Ile Ala Phe Leu Lys Lys	Leu Pro Ile Gin Thr Tyr Ser Ala Leu Asn Phe Arg Glu Thr Ser Pro
225 230 235 240	420 425 430
Val His Glu Glu Glu Ile Arg Glu Leu Gln Ala Gln Leu Gln Glu Gln .	Glu Gln Arg Gly Ser Glu Val His Thr Lys Lys Thr Val Met Ile Lys
20 245 250 255	20 435 440 445
Gin Val Gin Val Glu Met App Met Ser Lys Pro Asp Leu Thr Ala Ala	Thr Ile Glu Thr Arg Asp Gly Glu Val Val Ser Glu Ala Thr Gln Gln
260 265 270	450 455 460
Leu Arg Asp Ile Arg Ale Gin Tyr Glu Thr Ile Ale Ale Lys Asn Ile	Gln His Glu Vel Leu
275 280 285	465

WO 2004/055519	219/335	PCT/EP2003/014057	WO 2004/055519 220/335	PCT/EP2003/014057
			Leu Arg Asn Val Val Glu Ala Gln Phe Asp Ser Arg Val Arg Ala Thr	rg Ala Thr
			100 105	110
<210> 71			Gly His Ser Tyr Glu Lys Tyr Asn Lys Trp Glu Thr Ile Glu Ala Trp	lu Ala Trp
<211> 417		,	115 120 125	
5 <212> PRT			5 Thr Gln Gln Val Ala Thr Glu Asn Pro Ala Leu Ile Ser Arg Ser Val	ig Ser Val
<213> Homo sapiens	apiens		130 135 140	-
<2220>			ile Gly Thr Thr Phe Glu Gly Arg Ale ile Tyr Leu Leu Lys Vel Gly	s Val Gly
<221> Carbox	Carboxypeptidase B precursor		145 150 155	160
<222> (1)(417)	(417)		Lys Ala Gly Gln Asn Lys Pro Ala Ile Phe Met Asp Cys Gly Phe His	y Phe His
10 <223> Access.	Accession No. as of 29 August 2003: P15086		10 165 170	175
<400> 71			Ala Arg Glu Trp Ile Ser Pro Ala Phe Cys Gln Trp Phe Val Arg Glu	il Arg Glu
			180 185 190	9
Met Leu Ala L	Met Leu Ala Leu Leu Val Leu Val Thr Val Ala Leu Ala	la Ser Ala His	Ala Val Arg Thr Tyr Gly Arg Glu Ile Gln Val Thr Glu Leu Leu Asp	n Leu Asp
п	5 10	15	. 195 200 205	
15 His Gly Gly G	His Gly Gly Glu His Phe Glu Gly Glu Lys Val Phe Arg	rg Val Asn Val	15 Lys Leu Asp Phe Tyr Val Leu Pro Val Leu Asn Ile Asp Gly Tyr Ile	y Tyr Ile
20	0 25	30	210 215 220	
Glu Asp Glu A	Glu Asp Glu Asn His Ile Asn Ile ile Arg Glu Leu Ala	la Ser Thr Thr	Tyr Thr Trp Thr Lys Ser Arg Phe Trp Arg Lys Thr Arg Ser Thr His	r Thr His
35	40 45	ις.	225 230 235	240
Gln ile Asp Pl	Gin ile Asp Phe Txp Lys Pro Asp Ser Val Thr Gin Ile	le Lys Pro His	Thr Gly Ser Ser Cys Ile Gly Thr Asp Pro Asn Arg Asn Phe Asp Ala	e Asp Ala
. 20 50	. 09		20 245 250	255
Ser Thr Val A	Ser Thr Val Asp Phe Arg Val Lys Ala Glu Asp Thr Val Thr Val	al Thr Val Glu	Gly Trp Cys Glu Ile Gly Ala Ser Arg Asn Pro Cys Asp Glu Thr Tyr	u Thr Tyr
65	70 75	. 80	260 265 270	0
Asn Val Leu L	Asn Val Leu Lys Gln Asn Glu Leu Gln Tyr Lys Val Leu Ile Ser Asn	su lle Ser Asn	Cys Gly Pro Ala Ala Glu Ser Glu Lys Glu Thr Lys Ala Leu Ala Asp	u Ala Asp
	90	. 35	275 280 285	

WO 2004/055519 PCT/EP2003/014057 221/335	WO 2004/055519 PCT/EP2003/014057 222/335
Phe ile Arg Asn Lys Leu Ser Ser Ile Lys Ala Tyr Leu Thr Ile His	<2220>
290 295 300	<221> Carboxypeptidase Al precursor
Ser Tyr Ser Gln Met Met Ile Tyr Pro Tyr Ser Tyr Ala Tyr Lys Leu	<222>_ (1) (419)
305 310 315 320	<223> Accession No. as of 29 August 2003; P15085
5 Gly Glu Asn Asn Ala Glu Leu Asn Ala Leu Ala Lys Ala Thr Val Lys	5 <400> 72
325 330 335	
Glu Leu Ala Ser Leu His Gly Thr Lys Tyr Thr Tyr Gly Pro Gly Ala	Met Arg Gly Leu Leu Val Leu Ser Val Leu Leu Gly Ala Val Phe Gly
340 345 350	1 5 10 15
Thr Thr Ile Tyr Pro Ala Ala Gly Gly Ser Asp Asp Trp Ala Tyr Asp	Lys Glu Asp Phe Val Gly His Gln Val Leu Arg Ile Ser Val Ala Asp
10 355 360 365	10 20 25 30
Gln Gly Ile Arg Tyr Ser Phe Thr Phe Glu Leu Arg Asp Thr Gly Arg	Glu Ala Gln Vel Gln Lys Val Lys Glu Leu Glu Asp Leu Glu His Leu
370 375 380	35 40 45
Tyr Gly Phe Leu Leu Pro Glu Ser Gln Ile Arg Ala Thr Cys Glu Glu	Gin Leu Asp Phe Trp Arg Gly Pro Ala His Pro Gly Ser Pro Ile Asp
385 390 395 400	9 25 60
15 Thr Phe Leu Ala 11e Lys Tyr Val Ala Ser Tyr Val Leu Glu His Leu	15 Val Arg Val Pro Phe Pro Ser Ile Gln Ala Val Lys Ile Phe Leu Glu
405 410 415	. 65 70 75 80
Tyr	Ser His Gly Ile Ser Tyr Glu Thr Net Ile Glu Asp Vel Gln Ser Leu
	. 85 90 °C
	Leu Asp Glu Glu Glu Glu Gln Met Phe Ala Phe Arg Ser Arg Ala Arg
20	20 . 100 105 110
<210> 72	Ser Thr Asp Thr Phe Asn Tyr Ala Thr Tyr His Thr Leu Glu Glu Ile
<211> 419	115 120 125
<212> PRT	Tyr Asp Phe Leu Asp Leu Leu Val Ala Glu Asn Pro His Leu Val Ser
<213> Homo sapiens	130 135 140

WO 2004/055519	223/335	PCT/EP2003/014057		WO 2004/055519		224/335	PCT/EP2003/0140
Lys ile Gin ile Gly Asn Thr Tyr Glu Gly Arg Pro ile Tyr Val Leu	r Glu Gly Arg Pro Ile	Tyr Val Leu		. Val Thr Ala L	eu Ala Ser Leu Ty	Vel Thr Ale Leu Ale Ser Leu Tyr Gly Thr Lys Phe Asn Tyr Gly Ser	n Tyr Gly Ser
145 150	155	160			340	345	350
Lys Phe Ser Thr Gly Gly Ser Lys Arg Pro Ala Ile		Trp Ile Asp Thr		Ile Ile Lys A	la ile Tyr Gln Al	ile ile Lys Ala ile Tyr Gin Ala Ser Gly Ser Thr ile Asp Trp Thr	e Asp Trp Thr
165	170	175		355	360	365	ις.
Gly ile His Ser Arg Glu Trp Val Thr Gln Ala Ser		Gly Val Trp Phe		5 Tyr Ser Gln G	ly ile Lys Tyr Se	Tyr Ser Gin Gly Ile Lys Tyr Ser Phe Thr Phe Glu Leu Arg Asp Thr	u Arg Asp Thr
. 180	185	190		370	375	380	
Ala Lys Lys Ile Thr Gln Asp Tyr Gly Gln Asp Ala		Ala Phe Thr Ala		Gly Arg Tyr G	ly Phe Leu Leu Pr	Gly Arg Tyr Gly Phe Leu Leu Pro Ala Ser Gln 11e 11e Pro Thr Ala	e Pro Thr Ala
195 200	10 205			385	390	395	400
lle Leu Asp Thr Leu Asp Ile Phe Leu Glu Ile Val		Thr Asn Pro Asp		Lys Glu Thr T	ro Leu Ala Leu Le	Lys Glu Thr Try Leu Ala Leu Leu Thr Ile Met Glu His Thr Leu Aan	s Thr Leu Asn
210 215	220				405	410	415
Gly Phe Ala Phe Thr His Ser Thr Asn Arg Met Trp		Arg Lys Thr Arg		His Pro Tyr			
225 230	235	240					
Ser His Thr Ala Gly Ser Leu Cys Ile Gly Val Asp		Pro Asn Arg Asn					
245	250	. 255					
Trp Asp Ala Gly Phe Gly Leu Ser Gly Ala Ser Ser		Asn Pro Cys Ser		5 <210> 73			
260	265	270		<211> 418			
Glu Thr Tyr His Gly Lys Phe Ala Asn Ser Glu Val		Glu Val Lys Ser		<212> PRT			
275 280	0 285		,	<213> Homo sapiens	apiens		
Ile Val Asp Phe Val Lys Asp His Gly Asn Ile Lys		Ala Phe Ile Ser		. <220>			
290 295	300		20	/ <221> Colligin 2	in 2	٠	-
lle His Ser Tyr Ser Gln Leu Leu Met Tyr Pro Tyr		Gly Tyr Lys Thr		<222> (1)(418)	118)		٠
305 310	315	320	•	<223> Ассевя	lon No. as of 29 1	Accession No. as of 29 August 2003: P50454	
Glu Pro Val Pro Asp Gln Asp Glu Leu Asp Gln Leu		Ser Lys Ala Ala		<400> 73		·	
325	330	335					

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WO 2004/055519 PCT/EP2003/014057 225/335	WO 2004/055519 PCT/EP2003/014057
	C60/393
Met Arg Ser Leu Leu Leu Leu Ser Ala Phe Cys Leu Leu Glu Ala Ala	Glu Arg Thr Asp Gly Ala Leu Leu Val Asn Ala Met Phe Phe Lys Pro
1 5 10 15	195 200 205
Leu Ala Ala Glu Val Lys Lys Pro Ala Ala Ala Ala Ala Pro Gly Thr	His Trp Asp Glu Lys Phe His His Lys Mat Val Asp Asn Arg Gly Phe
20 25 30	210 215 220
5 Ala Glu Lys Leu Ser Pro Lys Ala Ala Thr Leu Ala Glu Arg Ser Ala	5 Met Val Thr Arg Ser Tyr Thr Val Gly Val Met Met Met His Arg Thr
35 40 45	225 230 235 240
Gly Leu Ala Phe Ser Leu Tyr Gln Ala Met Ala Lys Asp Gln Ala Val	Gly Leu Tyr Asn Tyr Tyr Asp Asp Glu Lys Glu Lys Leu Gln Ile Val
. 09 55 60	245 250 . 255
Glu Asn Ile Leu Val Ser Pro Val Val Ala Ser Ser Leu Gly Leu	Glu Met Pro Leu Ala His Lys Leu Ser Ser Leu Ile Ile Leu Met Pro
10 65 70 75 80	10 260 265 270
Val Ser Leu Gly Gly Lys Ala Thr Thr Ala Ser Gln Ala Lys Ala Val	His His Val Glu Pro Leu Glu Arg Leu Glu Lys Leu Leu Thr Lys Glu
	275 280 285
Leu Ser Ala Glu Gln Leu Arg Asp Glu Glu Val His Ala Gly Leu Gly	Gln Leu Lys Ile Trp Met Gly Lys Met Gln Lys Lys Ala Val Ala Ile
100 105 110	290 295 300
15 Glu Leu Leu Arg Ser Leu Ser Asn Ser Thr Ala Arg Asn Val Thr Trp	15 Ser Leu Pro Lys Gly Val Val Glu Val Thr His Asp Leu Gln Lys His
115 120 125	305 310 315 320
Lys Leu Gly Ser Arg Leu Tyr Gly Pro Ser Ser Val Ser Phe Ala Asp	Leu Ala Gly Leu Gly Leu Thr Glu Ala Ile Asp Lys Asn Lys Ale Asp
130 135 140	325 330 335
Asp Phe Val Arg Ser Eys Gln His Tyr Asn Cys Glu His Ser Lys	Leu Ser Arg Met Ser Gly Lys Lys Asp Leu Tyr Leu Ala Ser Val Phe
20 145 150 155 160	20 340 345 350
lle Asn Phe Arg Asp Lys Arg Ser Ala Leu Gln Ser Ile Asn Glu Trp	His Ala Thr Ala Phe Glu Leu Asp Thr Asp Gly Asn Pro Phe Asp Gln
165 170 175	355 360 365
Ala Ala Gin Thr Thr Asp Gly Lys Leu Pro Glu Val Thr Lys Asp Val	Amp lle Tyr Gly Arg Glu Glu Leu Arg Ser Pro Lym Leu Phe Tyr Ala
. 180 185 190	370 375 380

WO 2004/055519			
227/335	LC ITET 2005/01405/	WO 2004/035519 PCT/EP2003/014057 228/335	03/014057
Asp His Pro Phe Ile Phe Leu Val Arg Asp Thr Gln Ser	Gln Ser Gly Ser Leu	Val Ser Leu Gln Asp Lys Thr Gly Phe His Phe Cys Gly Gly Ser Leu	3
385 390 395	400	50 55 60	
Leu Phe Ile Gly Arg Leu Val Arg Pro Lys Gly Asp Lys	Asp Lys Met Arg Asp	Ile Ser Glu Asp Trp Val Val Thr Ala Ala His Cys Gly Val Arg Thr	h
405 410	415	65 70 75 80	
Glu Leu		5 Ser Asp Val Val Val Ala Gly Glu Phe Asp Gln Gly Ser Asp Glu Glu	J
		. 06 28 .	
		Asn Ile Gln Val Leu Lys Ile Ala Lys Val Phe Lys Asn Pro Lys Phe	•
		100 105 110	
<210> 74		Ser lle Leu Thr Val Asn Asn Asp lle Thr Leu Leu Lys Leu Ala Thr	S.
<211> 263		10 115 120 125	
- <212> PRT		Pro Ala Arg Phe Ser Gln Thr Val Ser Ala Val Cys Leu Pro Ser Ala	est
<213> Homo sapiens		130 135 140	
<220>		Asp Asp Phe Pro Ala Gly Thr Leu Cys Ala Thr Thr Gly Trp Gly	
<221> Chymotrypsinogen B precursor		145 150 155 160	
<222> (1)(263)		15 Lys Thr Lys Tyr Asn Ala Asn Lys Thr Pro Asp Lys Leu Gln Gln Ala	ស
<223> Accession No. as of 29 August 2003; P17538	P17538	165 170 175	
<400> 74		Ala Leu Fro Leu Leu Ser Asn Ala Glu Cys Lys Lys Ser Trp Gly Arg	b
		180 185 190	
Met Ala Phe Leu Trp Leu Leu Ser Cys Trp Ala Leu Leu Gly Thr Thr	Leu Leu Gly Thr Thr	Arg Ile Thr Asp Val Met Ile Cys Ala Gly Ala Ser Gly Val Ser Ser	٠.
1 5 10	. 15	20 195 200 205	
Phe Gly Cys Gly Val Pro Ala Ile His Pro Val Leu Ser Gly Leu Ser	Leu Ser Gly Leu Ser	Cys Met Gly Asp Ser Gly Gly Pro Leu Val Cys Gln Lys Asp Gly Ala	æ
20 25	30	210 215 220	
Arg lle Val Asn Gly Glu Asp Ala Val Pro Gly Ser Trp Pro Trp Gln	Ser Trp Pro Trp Gln	Trp Thr Leu Val Gly 11e Val Ser Trp Gly Ser Asp Thr Cys Ser Thr	
35 40	45	225 230 235 240	·

WO 2004/055519 229/335	PCT/EP2003/014057	WO 2004/055519 PCT/EP2003/014057 230/335
Ser Ser Pro Gly Val Tyr Ala Arg Val Thr Lys Leu Ile P	eu Ile Pro Trp Val	Tyr Lys Ser Arg Ile Gln Val Arg Leu Gly Glu His Asn Ile Glu Val
245 250	255	65 70 75 80
Gln Lys Ile Leu Ala Ala Asn		Leu Glu Gly Asn Glu Gln Phe Ile Asn Ala Ala Lys Ile Ile Arg His
· · ·		5 Pro Gln Tyr Asp Arg Lys Thr Leu Asn Asn Asp Ile Met Leu Ile Lys
		100 105 110
<210> 75		Leu Ser Ser Arg Ala Val Ile Asn Ala Arg Val Ser Thr Ile Ser Leu
<211> 247		115 120 125
<212> PRT	-	Pro Thr Ala Pro Pro Ala Thr Gly Thr Lys Cys Leu Ile Ser Gly Trp
10 <213> Homo sapiens		10 130 135 140
<220>		Gly Asn Thr Ala Ser Gly Ala Asp Tyr Pro Asp Glu Leu Gln Cys
<221> Trypsin I precursor		145 150 155 160
<222> (1)(247)		Leu Asp Ala Pro Val Leu Ser Gln Ala Lys Cys Glu Ala Ser Tyr Pro
<223> Accession No. as of 29 August 2003: P07477	7477	165 170 175
15 <400> 75		15 Gly Lys Ile Thr Ser Asn Met Phe Cys Val Gly Phe Leu Glu Gly Gly
		180 185 190
Met Asn Pro Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Leu Ala Ala	la Ala Leu Ala Ala	Lys Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Val Val Cys Asn Gly
1 5 10	15	195 200 205
Pro Phe Asp Asp Asp Lys Ile Val Gly Gly Tyr Asn Cys Glu Glu	yr Asn Cys Glu Glu	Gln Leu Gln Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gln Lys Asn
20 25	30 ·	20 210 215 220
Asn Ser Val Pro Tyr Gln Val Ser Leu Asn Ser Gly Tyr His Phe Cys	ly Tyr His Phe Cys	Lys Pro Gly Val Tyr Thr Lys Val Tyr Asn Tyr Val Lyg Trp Ile Lys
35 40	45	225 230 235 240
Gly Gly Ser Leu Ile Asn Glu Gln Trp Val Val Ser Ala Gly His Cys	er Ala Gly His Cys	Asn Thr Ile Ala Ala Asn Ser
99 \$5 05	0	245

WO 2004/055519	_	PCT/EP2003/014057		WO 2004/055519 PCT/RP	PCT/EP2003/014057
231/335				232/335	
				Pro Lys Tyr Asn Ser Arg Thr Leu Asp Asn Asp Ile Leu Leu Ile Lys	Lys
				100 105 110	٠.
<210> 76				Leu Ser Ser Pro Ala Val Ile Asn Ser Arg Val Ser Ala: Ile Ser Leu	геп
<211> 247				115 120 125	
5 <212> PRT			•	5 Pro Thr Ala Pro Pro Ala Ala Gly Thr Glu Ser Leu Ile Ser Gly Trp	Trp
<213> Homo sapiens				130 135 140	
<220>				Gly Asn Thr Leu Ser Ser Gly Ala Asp Tyr Pro Asp Glu Leu Gln Cys	Сув
<221> Trypsin II precursor				145 150 155	160
<222> (1)(247)				Leu Asp Ala Pro Val Leu Ser Gln Ala Glu Cys Glu Ala Ser Tyr Pro	Pro
10 <223> Accession No. as of 29 August 2003: P07478	: 2003: P07478		01	0 165 170 175	
<400> 76				Gly Lys Ile Thr Asn Asn Met Phe Cys Val Gly Phe Leu Glu Gly Gly	31 <i>y</i>
				. 180 185 190	
Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala		Val Ala Ala		Lys Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Val Val Ser Asn Gly	313
	10	15		200 205	
15 Pro Phe Asp Asp Asp Lys Ile Val Gly Gly Tyr Ile		Cys Glu Glu	==	15 Glu Leu Gln Gly 11e Val Ser Trp Gly Tyr Gly Cys Ala Gln Lys Asn	Asn
20 25	30			210 215 220	
Asn Ser Val Pro Tyr Gln Val Ser Leu Asn Ser Gly Tyr		His Phe Cys		Arg Pro Gly Val Tyr Thr Lys Val Tyr Asn Tyr Val Asp Trp Ile Lys	Ly a
35 40	45			225 230 235 2	240
Gly Gly Ser Leu Ile Ser Glu Gln Trp Val Val Ser Ala Gly His Cys	Val Val Ser Ala Gly	His Cys		Asp Thr ile Ala Ala Aen Ser	
20 50 . 55	09		20	0 245	
Tyr Lys Ser Arg Ile Gln Val Arg Leu Gly Glu His Asn Ile Glu Val	Gly Glu His Asn Ile	Glu Val			
	75				
Leu Glu Gly Asn Glu Gln Phe Ile Asn Ala Ala Lys Ile Ile Arg His	Ala Ala Lys Ile Ile	Arg His		<210> 77	
88	06	. 26		<211> 379	

	WO 2004/055519	PCT/FD2003/014057	WO 2004/055519	PCT/FP2003/014057
	233/335			234/335
	<212> PRT		Arg Lys Thr Ile Asn Gln	Arg Lys Thr Ile Asn Gln Trp Val Lys Gly Gln Thr Glu Gly Lys Ile
	<213> Homo sapiens		130	135 140
	<220>		Pro Glu Leu Leu Ala Ser (Pro Glu Leu Leu Ala Ser Gly Met Val Asp Asn Met Thr Lys Leu Val
	<221> Leukocyte elastase inhibitor (LEI)		145 150	. 155 160
5	<222> (1)(379)	,	5 Leu Val Asn Ala Ile Tyr 1	Leu Val Asn Ala Ile Tyr Phe Lys Gly Asn Trp Lys Asp Lys Phe Met
	<223> Accession No. as of 29 August 2003: P30740	930740	. 165	170 175
	<400> 77		Lys Glu Ala Thr Thr Asn	Lys Glu Ala Thr Thr Asn Ala Pro Phe Arg Leu Asn Lys Lys Asp Arg
			. 180	185
•	Met Glu Gln Leu Ser Ser Ala Asn Thr Arg Phe Ala Leu	Ala Leu Asp Leu Phe	Lys Thr Val Lys Met Met 1	Lys Thr Val Lys Met Met Tyr Gln Lys Lys Phe Ala Tyr Gly Tyr
2	1 5 10	15	195	200 205
	Leu Ala Leu Ser Glu Asn Asn Pro Ala Gly Asn Ile Phe	Ile Phe Ile Ser Pro	Ile Glu Asp Leu Lys Cys ?	Ile Glu Asp Leu Lys Cys Arg Val Leu Glu Leu Pro Tyr Gln Gly Glu
	20 25	30	210	215 220
	Phe Ser Ile Ser Ser Ala Met Ala Met Val Phe Leu Gly	Leu Gly Thr Arg Gly	Glu Leu Ser Met Val Ile I	Glu Leu Ser Met Val Ile Leu Leu Pro Asp Asp Ile Glu Asp Glu Ser
	35 40		. 225 230	235 240
15	Asn Thr Ala Ala Gln Leu Ser Lys Thr Phe His Phe Asn	Phe Asn Thr Val Glu	15 Thr Gly Leu Lys Lys Ile (Thr Gly Leu Lys Lys Ile Glu Glu Gln Leu Thr Leu Glu Lys Leu His
	50 55	09	245	250 255
	Glu Val His Ser Arg Phe Gln Ser Leu Asn Ala Asp Ile	Asp Ile Asn Lys Arg	Glu Trp Thr Lys Pro Glu	Glu Trp Thr Lys Pro Glu Asn Leu Asp Phe Ile Glu Val Asn Val Ser
	65 70 75	08	260	265 270
	Gly Ala Ser Tyr Ile Leu Lys Leu Ala. Asn Arg Leu Tyr	Leu Tyr Gly Glu Lys		Leu Pro Arg Phe Lys Leu Glu Glu Ser Tyr Thr Leu Asn Ser Asp Leu
20	85		20 275	280 285
	Thr Tyr Asn Phe Leu Pro Glu Phe Leu Val Ser Thr Gln	Thr Gln Lys Thr Tyr	Ala Arg Leu Gly Val Gln	Ala Arg Leu Gly Val Gln Asp Leu Phe Asn Ser Ser Lys Ala Asp Leu
	. 100 105	110	. 290	300
	Gly Ala Asp Leu Ala Ser Val Asp Phe Gln His Ala Ser	Ala Ser Glu Asp Ala.	Ser Gly Met Ser Gly Ala	Ser Gly Met Ser Gly Ala Arg Asp Ile Phe Ile Ser Lys Ile Val His
•	115 120	125	305 310	315 320

5	WO 2004/055519	235/335	PCT/EP2003/014057		WO 2004/055519	PCT/EP2003/0
	Lys Ser Phe Val Glu Vai	Lys Ser Phe Val Glu Val Asn Glu Glu Gly Thr Glu Ala Ala Ala Al	lu Ala Ala Ala		Gly Ala Asp Ala Arg Ala Le	Gly Ala Asp Ala Arg Ala Leu Met Leu Gln Gly Val Asp Leu Leu Ala
	. 325	330	335		35	40 45
	Thr Ala Gly Ile Ala Thi	Thr Ala Gly Ile Ala Thr Phe Cys Met Leu Met Pro Glu Glu Asn Phe	ro Glu Glu Asn Phe		Asp Ala Val Ala Val Thr Me	Asp Ala Val Ala Val Thr Met Gly Pro Lys Gly Arg Thr Val Ile Ile
	340	345	350		50	. 09
'n	Thr Ala Asp His Pro Phe	Thr Ala Asp His Pro Phe Leu Phe Phe Ile Arg His Asn Ser Ser	is Asn Ser Ser Gly		5 Glu Gln Ser Trp Gly Ser Pr	Glu Gln Ser Trp Gly Ser Pro Lys Val Thr Lys Asp Gly Val Thr Val
,	355	360	365	*	92	75 80
-	Ser Ile Leu Phe Leu Gly Arg Phe Ser Ser Pro	Arg Phe Ser Ser Pro			Ala Lys Ser Ile Asp Leu Ly	Ala Lys Ser Ile Asp Leu Lys Asp Lys Tyr Lys Asn Ile Gly Ale Lys
	370	375			រភ 80	96 06
		٠.			Leu Val Gln Asp Val Ala Ass	Leu Val Gin Asp Val Ala Asn Asn Thr Asn Glu Giu Ala Gly Asp Gly
10					. 10 100	105 110
•	<210> 78				Thr Thr Thr Ala Thr Val Lev	Thr Thr Thr Ala Thr Val Leu Ala Arg Ser Ile Ala Lys Glu Gly Phe
•	<211> 573				115	120 125
•	<212> PRT	·	,		Glu Lys Ile Ser Lys Gly Ale	Glu Lys Ile Ser Lys Gly Ala Asn Pro Val Glu Ile Arg Arg Gly Val
*	<213> Homo sapiens				130 135	140
15	<220>				15 Met Leu Ala Val Asp Ala Val	Met Leu Ala Val Asp Ala Val Ile Ala Glu Leu Lys Lys Gln Ser Lys
	<221> нвр60				145 150	155 160
•	<222> (1) (573)				Pro Val Thr Thr Pro Glu Glu	Pro Val Thr Thr Pro Glu Glu lie Ala Gln Val Ala Thr Ile Ser Ala
٧	<223> Accession No. as	Accession No. as of 29 August 2003; P10	9809		165	170 175
٧	<400> 78				Asn Gly Asp Lys Glu Ile Gly	Asn Gly Asp Lys Glu Ile Gly Asn Ile Ile Ser Asp Ala Met Lys Lys
70					20 .180	185
¥	Met Leu Arg Leu Pro Thr Val Phe Arg Gln Met Ar	Val Phe Arg Gln Met Arg	g Pro Val Ser Arg		Val Gly Arg Lys Gly Val Ile	Val Gly Arg Lys Gly Val Ile Thr Val Lys Asp Gly Lys Thr Leu Asn
ri	ហ	10	15		195	200 205
>	al Leu Ala Pro His Leu	Val Leu Ala Pro His Leu Thr Arg Ala Tyr Ala Lys Asp Val Lys Phe	s Asp Val Lys Phe		Asp Glu Leu Glu Ile Ile Glu	Asp Glu Leu Glu Ile Ile Glu Gly Met Lys Phe Asp Arg Gly Tyr Ile
	20	25	30		210 215	

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WO 200	WO 2004/055519	237/335	.vo	PCT/EP2003/014057	WO 2004/055519	PCT/EP2003/014057	0\$7
Ser	Pro Tyr Phe Ile	Asn Thr Ser Lys	Ser Pro Tyr Phe 11e Asn Thr Ser Lys Gly Gln Lys Cys	Glu Phe Gln	Lys Lys Asp Arg Val Thr Asp	LYS LYS ASP Arg Val Thr Asp Ala Leu Asn Ala Thr Arg Ala Ala Val	
225		230	235	240	420	425 430	
Asp	Ala Tyr Val Leu	Leu Ser Glu Lys	Asp Ala Tyr Val Leu Leu Ser Glu Lys Lys Ile Ser Ser	Ile Gln Ser	Glu Glu Gly Ile Val Leu Gly	Glu Glu Gly Ile Val Leu Gly Gly Gly Cys Ala Leu Leu Arg Cys Ile	
	245		250		435	440 445	
5 Ile	Val Pro Ala Leu	Glu Ile Ala Asn	lle Val Pro Ala Leu Glu Ile Ala Asn Ala His Arg Lys	Pro Leu Val	5 Pro Ala Leu Asp Ser Leu Thr	Pro Ala Leu Asp Ser Leu Thr Pro Ala Asn Glu Asp Gln Lys Ile Gly	
	. 560	. 265		270	450 455	460	
Ile	Ile Ala Glu Asp	Val Asp Gly Glu	Ile Ile Ala Glu Asp Val Asp Gly Glu Ala Leu Ser Thr	Leu Val Leu	ile Glu ile ile Lys Arg Thr	ile Glu ile ile Lys Arg Thr Leu Lys Ile Pro Ala Met Thr Ile Ala	
	275	280	285		465	475 480	
Asn 1	Arg Leu Lys Val	Gly Leu Gln Val	Asn Arg Leu Lys Val Gly Leu Gln Val Val Ala Val Lys)	Ala Pro Gly	Lys Asn Ala Gly Val Glu Gly	Lys Asn Ala Gly Val Glu Gly Ser Leu Ile Val Glu Lys Ile Met Gln	
10	290	295	300		10 485	490 495	
Phe (Gly Asp Asn Arg	Lys Asn Gln Leu	Phe Gly Asp Asn Arg Lys Asn Gln Leu Lys Asp Met Ala 1	Ile Ala Thr	Ser Ser Ser Glu Val Gly Tyr	Ser Ser Glu Val Gly Tyr Asp Ala Met Ala Gly Asp Phe Val Asn	
305		310	315	320	. 200	505 510	
Gly (3ly Ala Val Phe	Gly Glu Glu Gly	Gly Gly Ala Val Phe Gly Glu Glu Gly Leu Thr Leu Asn I	Leu Glu Asp	. Met Val Glu Lys Gly Ile Ile	Met Val Glu Lys Gly Ile Ile Asp Pro Thr Lys Val Val Arg Thr Ala	
	325		330	335	. 515	520 525	
15 Val G	3ln Pro His Asp	Leu Gly Lys Val	Val Gln Pro His Asp beu Gly Lys Val Gly Glu Val Ile Val Thr Lys		15 Leu Leu Asp Ala Ala Gly Val	Leu Leu Asp Ala Ala Gly Val Ala Ser Leu Leu Thr Thr Ala Glu Val	
	340	345		350	530 535	540	
Asp A	Asp Ala Met Leu	Leu Lys Gly Lys	Asp Asp Ala Met Leu Leu Lys Gly Lys Gly Asp Lys Ala G	Gln ile Glu	Val Val Thr Glu Ile Pro Lys	Val Val Thr Glu lle Pro Lys Glu Glu Lys Asp Pro Gly Met Gly Ala	
	355	360	365		545 550	. 555	
Гув А	irg Ile Gln Glu	Ile Ile Glu Gln	Lys Arg Ile Gln Glu Ile Ile Glu Gln Leu Asp Val Thr Thr Ser Glu	thr Ser Glu	Met Gly Gly Met Gly Gly Gly Met Gly Gly Gly Met Phe	Met Gly Gly Gly Met Phe	
20 3	370	375	380	7	20 565	.570	
Tyr 6	ilu Lys Glu Lys	Leu Asn Glu Arg	Tyr Glu Lys Glu Lys Leu Asn Glu Arg Leu Ala Lys Leu Ser Asp Gly	er Asp Gly			
385	•	390	395	400			
Val A	la Val Leu Lys	Val Gly Gly Thr	Val Ala Val Leu Lys Val Gly Gly Thr Ser Asp Val Glu V	Al Asn Glu	<210> 79		
	405		410	415	<211> 803	-	

WO 2004/055519 PCT/EP2003/014057	Asn Glu Glu Leu Thr Val Lys Ile Lys Cys Asp Lys Glu Lys Asn Leu	130 135 140	Leu His Val Thr Asp Thr Gly Val Gly Met Thr Arg Glu Glu Leu Val	145 150 155 160	5 Lys Asn Leu Gly Thr Ile Ale Lys Ser Gly Thr Ser Glu Phe Leu Asn	165 170 175	Lys Met Thr Glu Ala Glu Asp Gly Gln Ser Thr Ser Glu Leu Ile	180 185 190	Gly Gln Phe Gly Val Gly Phe Tyr Ser Ala Phe Leu Val Ala Asp Lys	10 195 200 205	Val 11e Val Thr Ser Lys His Asn Asn Asp Thr Gln His 11e Trp Glu	210 215 220	Ser Asp Ser Asn Glu Phe Ser Val Ile Ala Asp Pro Arg Gly Asn Thr	225 230 235 240	15 Leu Gly Arg Gly Thr Thr Ile Thr Leu Val Leu Lys Glu Glu Ala Ser	245 250 255	Asp Tyr Leu Glu Leu Asp Thr Ile Lys Asn Leu Val Lys Lys Tyr Ser	260 265 270	Gin Phe ile Asn Phe Pro ile Tyr Val Trp Ser Sex Lys Thr Glu Thr	20 275 280 285	Val Glu Glu Pro Met Glu Glu Glu Glu Ala Ala Lys Glu Glu Lys Glu	290 295 300	Glu Ser Asp Asp Glu Ala Ala Val Glu Glu Glu Glu Glu Lys Lys	305 .310 315 320
WO 2004/055519 PCT/EP2003/014057	<212> PRT	<213> Homo sapiens	<220>	<221> Endoplasmin precursor (GRP94)	5 <222> (1)(803)	<223> Accession No. as of 29 August 2003: P14625	<400> 79		Met Arg Ala Leu Trp Val Leu Gly Leu Cys Cys Val Leu Leu Thr Phe	10 1 5 10 15	Gly Ser Val Arg Ala Asp Asp Glu Val Asp Val Asp Gly Thr Val Glu	20 25 30	Glu Asp Leu Gly Lys Ser Arg Glu Gly Ser Arg Thr Asp Asp Glu Val	35 40 45	15 Val Gln Arg Glu Glu Ala Ile Gln Leu Asp Gly Leu Asn Ala Ser		Gln ile Arg Glu Leu Arg Glu Lys Ser Glu Lys Phe Ala Phe Gln Ala	65 70 75 80	Glu Val Asn Arg Met Met Lys Leu Ile Ile Asn Ser Leu Tyr Lys Asn		Lys Glu Ile Phe Leu Arg Glu Leu Ile Ser Asn Ala Ser Asp Ala Leu	100 105 110	Asp Lys lle Arg Leu lle Ser Leu Thr Asp Glu Asn Ala Leu Ser Gly	115 120 125

. WO 2004/055519 PCT/E	PCT/EP2003/014057	WO 2004/053519 PCT/EP2003/0:
Pro Lys Thr Lys Lys Val Glu Lys Thr Val Trp Asp Trp Glu Leu Met	Met	Gln Ser Ser His His Pro Thr Asp Ile Thr Ser Lan Ash Cln mer 150
325 330 335		515 520 626
Asn Asp Ile Lys Pro Ile Trp Gln Arg Pro Ser Lys Glu Val Glu Glu	Glu	Lys Glu Lys Gln Asp Lys Ile Tyr Phe
340 345 350		530 535 540
5 Asp Glu Tyr Lys Ala Phe Tyr Lys Ser Phe Ser Lys Glu Ser Asp Asp	Авр	Ser Arg Lys Glu Ala Glu Ser Ser Pro Phe Val Glu Arg Leu Leu Lys
355 360 365		545 550 555 560
Pro Met Ala Tyr Ile His Phe Thr Ala Glu Gly Glu Val Thr Phe Lys	Lys	Lys Gly Tyr Glu Val Ile Tyr Leu Thr Glu Pro Val Asp Glu Tyr Cys
370 375 380		565 570 575
Ser Ile Leu Phe Val Pro Thr Ser Ala Pro Arg Gly Leu Phe Asp Glu	Glu	Ile Gin Ala Leu Pro Glu Phe Asp Gly Lys Arg Phe Gin Asn Val Ala
10 385 390 395	400 10	585 585 585
Tyr Gly Ser Lys Lys Ser Asp Tyr Ile Lys Leu Tyr Val Arg Arg Val	Val	Lys Glu Gly Val Lys Phe Asp Glu Ser Glu Lys Thr Lys Glu Ser Ard
405 410 415		909 009 565
Phe Ile Thr Asp Asp Phe Hie Asp Met Met Pro Lys Tyr Leu Asn Phe	Phe	Glu Ala Val Glu Lys Glu Phe Glu Pro Leu Leu Asn Trp Met Lys Asn
420 425 430		610 615 620
15 Val Lys Gly Val Val Asp Ser Asp Asp Leu Pro Leu Asn Val Ser Arg	Arg IS	Lys Ala Leu Lys Asp Lys Ile Glu Lys Ala Val Val Ser Gln Arr Leu
435 440 445		625 630 635 640
Glu Thr Leu Gln Gln His Lys Leu Leu Lys Val Ile Arg Lys Leu	ner	Thr Glu Ser Pro Cys Ala Leu Val Ala Ser Gln Tyr Gly Trp Ser Gly
450 455 460		645 650 655
Val Arg Lys Thr Leu Asp Met Ile Lys Lys Ile Ala Asp Asp Lys T	Tyr	Asn Met Glu Arg Ile Met Lys Ala Gln Ala Tyr Gln Thr Gly Lys Asp
20 465 470 475 4	480 20	660 665 670
Asn Asp Thr Phe Trp Lys Glu Phe Gly Thr Asn Ile Lys Leu Gly Val	al	Ile Ser Thr Asn Tyr Tyr Ala Ser Gln Lys Lys Thr Phe Glu Ile Asn
485 490 495		675 680 685
ile Glu Asp His Ser Asn Arg Thr Arg Leu Ala Lys Leu Leu Arg Phe	ь	Pro Arg His Pro Leu Ile Arg Asp Met Leu Arg Arg Ile Lys Glu Asp
500 505 510		690 695 700

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WO 2004/055519 PCT/EP2003/014057 243/335	WO 2004/055519 PCT/EP2003/0 244/335
Glu Asp Asp Lys Thr Val Leu Asp Leu Ala Val Val Leu Phe Glu Thr	<400>
705 710 715 720	
Ala Thr Leu Arg Ser Gly Tyr Leu Leu Pro Asp Thr Lys Ala Tyr Gly	Met Ala Ala Ala Val Pro Arg Ala Ala Phe Leu Ser Pro Leu Leu Pro
725 730 735	1 5 10 15
Asp Arg Ile Glu Arg Met Leu Arg Leu Ser Leu Ann Ile Asp Pro Asp	5 Leu Leu Leu Gly Phe Leu Leu Ser Ala Pro His Gly Gly Ser Gly
740 745 750	. 20 25 . 30
Ala Lys Val Glu Glu Glu Bro Glu Glu Glu Pro Glu Glu Thr Ala Glu	Leu His Thr Lys Gly Ala Leu Pro Leu Asp Thr Val Thr Phe Tyr Lys
755 760 765	35 40 45
Asp Thr Thr Glu Asp Thr Glu Gln Asp Glu Asp Glu Glu Met Asp Vel	Val Ile Pro Lys Ser Lys Phe Val Leu Val Lys Phe Asp Thr Gln Tyr
770 . 775 780	
Gly Thr Asp Glu Glu Glu Thr Ala Lys Glu Ser Thr Ala Glu Lys	Pro Tyr Gly Glu Lys Gln Asp Glu Phe Lys Ary Leu Ala Glu Asn Ser
785 790 795 800	65 70 75 80
Asp Glu Leu	Ala Ser Ser Asp Asp Leu Leu Val Ala Glu Val Gly Ile Ser Asp Tyr
	56 06 58
	15 Gly App Lys Leu Asn Met Glu Leu Ser Glu Lys Tyr Lys Leu Asp Lys
	100 105 110
<210> 80	Glu Ser Tyr Pro Val Phe Tyr Leu Phe Arg Asp Gly Asp Phe Glu Asn
<211> 261	115 120 125
<212> PRT	Pro Val Pro Tyr Thr Gly Ala Val Lys Val Gly Ala Ile Gln Arg Trp
<21.3> Homo sapiens	20 130 135 140
<2220>	Leu Lys Gly Gln Gly Val Tyr Leu Gly Met Pro Gly Cys Leu Pro Val
<221> Endoplasmic reticulum protein ERp29 precursor (ERp31)(ERp28)	145 150 155 160
<222> (1) . (261)	Tyr Asp Ala Leu Ala Gly Glu Phe Ile Arg Ala Ser Gly Val Glu Ala
<223> Accession No. as of 29 August 2003; P30040	165 170 175
	•

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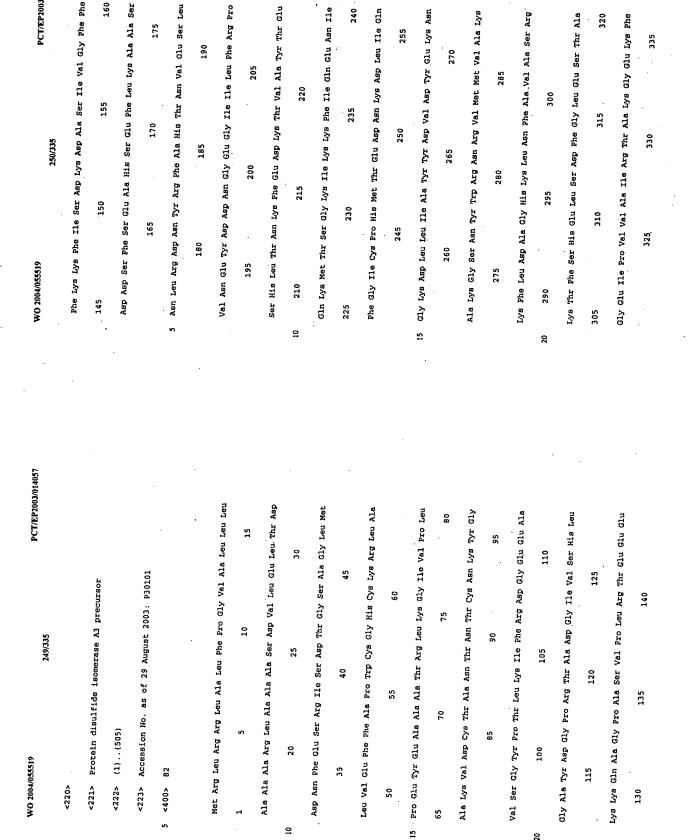
PCT/EP2003/014057

20

PCT/EP2003/014057 WO 2004/055519 246/335	Lys Met Ser Arg Gln Leu	. 1 5 10	Ser Cys Pro Trp Gly Gln Glu Gln Gly Ala Arg Ser Pro Ser Glu Glu	20 25	Ile 5 Pro Pro Glu Glu Glu Ile Pro Lys Glu Asp Gly Ile Leu Val Leu	35 . 40	Arg His Thr Leu Gly Leu Ala Leu Arg Glu His Pro	240 55 60	la Glu Phe Tyr Ala Pro Trp Cys Gly His Cys Gln Ala Leu Ala Pro Glu	10 65 70 75	Tyr Ser Lys Ala Ala Ala Val Leu Ala Ala Glu Ser Met Val Val Thr	. 06 58 .	Leu Ala Lys Val Asp Gly Pro Ala Gln Arg Glu Leu Ala Glu Glu Phe	100 105 110	15 Gly Val Thr Glu Tyr Pro Thr Leu Lys Phe Phe Arg Asn Gly Asn Arg	115 120 125	Thr His Pro Glu Glu Tyr Thr Gly Pro Arg Asp Ala Glu Gly Ile Ala	130 135 140	Glu Trp Leu Arg Arg Arg Val Gly Pro Ser Ala Met Arg Leu Glu Asp	20 145 150 155	Glu Ala Ala Ala Gln Ala Leu Ile Gly Gly Arg Asp Leu Val Val Ile	165 170
PCT/EP2 245/335	Arg Gln Ala Leu Leu Lys Gln Gly Gln Asp Asn Leu Ser Ser Val L	. 185	Glu Thr Gln Lys Lys Trp Ala Glu Gln Tyr Leu Lys Ile Met Gly Lys	200 205	Ile Leu Asp Gln Gly Glu Asp Phe Pro Ale Ser Glu Met Thr Arg Il	220	Ale Arg Leu Ile Glu Lys Asn Lys Met Ser Asp Gly Lys Lys Glu Glu	235 24	Leu Gln Lys Ser Leu Asn Ile Leu Thr Ala Phe Gln Lys Lys Gly Ala	250 255										Protein disulfide isomerase A2 precursor		<223> Accession No. as of 29 August 2003: Q13087
	u Lys Gln G		ys Trp Ala G	7	ly Glu Asp P	215	Hu Lys Asn L	230	eu Asn Ile Le	245	Glu Lys Glu Glu Leu							<213> Homo sapiens		sulfide isome	(1)(525)	No. as of 29

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	WO 2004/055519	300/070		PCT/EP2003/014057	-	*	WO 2004/055519			PCT/EP2003/014057	52
		2001147						24	248/335		
	Leu Ala Gln Asp Ala Leu Asp Met Thr Phe Gly Leu Thr	u Asp Met Thr Phe		Asp Arg Pro			Trp Asp Gln Arg P	ro Val Lys Thr	Trp Asp Gln Arg Pro Val Lys Thr Leu Val Gly Lys Asn Phe Glu Gln	n Phe Glu Gln	
	195	200	205				385	390	395	400	
	Arg Leu Phe Gin Gin Phe Gly Leu Thr Lys Asp Thr Val	s Gly Leu Thr Lys		Val Leu Phe			Val Ala Phe Asp G	lu Thr Lys Asn	Val Ala Phe Asp Glu Thr Lys Asn Val Phe Val Lys Phe Tyr Ala Pro	e Tvr Ala Pro	
	210	215	220				14	405	410	415	
s.	Lys Lys Phe Asp Glu Gly Arg Ala Asp Phe Pro Val Asp	Arg Ala Asp Phe		Glu Glu Leu		ľΩ	Trp Cys Thr His C	78 Lys Glu Met 2	Trp Cys Thr His Cys Lys Glu Met Ala Pro Ala Trp Glu Ala Len ala	u Ala Len Ala	
٠	225 230	·_	235	240			420		425	430	
	Gly Leu Asp Leu Gly Asp Leu Ser Arg Phe Leu Val Thr	Leu Ser Arg Phe		His Ser Met	•		Glu Lys Tyr Gln A	ip His Glu Asp'l	Glu Lys Tyr Gln Asp His Glu Asp Ile Ile Ile Als Glu Leu Asp Ala	i Leu Asp Ala	
	245	250		255			435	440	445		
	Arg Leu Val Thr Glu Phe Asn Ser Gln Thr Ser Ala Lys	Asn Ser Gln Thr		Ile Phe Ala		-	Thr Ala Asn Glu Le	u Asp Ala Phe A	Thr Ala Asn Glu Leu Asp Ala Phe Ala Val His Gly Phe Pro Thr Leu	Pro Thr Leu	
01	. 560	265	270			10	450	455	460		
	Ala Arg Ile Leu Asn His Leu Leu Leu Phe Val Asn Gin Thr Leu Ala	Leu Leu Leu Phe	Val Asn Gln Thr	Leu Ala		-	Lys Tyr Phe Pro Al	a Gly Pro Gly A	Lys Tyr Phe Pro Ala Gly Pro Gly Arg Lys Val Ile Glu Tyr Lys Ser	Tyr Lys Ser	
	275	280	285			. *	465	470	475	480	
	Ala His Arg Glu Leu Leu Ala Gly Phe Gly Glu Ala Ala Pro Arg Phe	Ala Gly Phe Gly	Glu Ala Ala Pro	Arg Phe		.,	Thr Arg Asp Leu Gl	u Thr Phe Ser L	Thr Arg Asp Leu Glu Thr Phe Ser Lys Phe Leu Asp Asn Gly Gly Val	Gly Gly Val	
	290	295	300				485	រភ	490	495	
15	Arg Gly Gln Val Leu Phe Val Val Val Asp Val Ala Ala Asp Asn Glu	Val Val Val Asp V	Val Ala Ala Asp	Asn Glu		15 1	eu Pro Thr Glu Gl	u Pro Pro Glu G	Leu Pro Thr Glu Glu Pro Pro Glu Glu Pro Ala Ala Pro Phe Pro Glu	Phe Pro Glu	-
	305 310	,	315	320			200	LG.	505	510	
	His Val Leu Gin Tyr Phe Gly Leu Lys Ala Giu Ala Ala Pro Thr Leu	Gly Leu Lys Ala	Glu Ala Ala Pro	Thr Leu			Pro Pro Ala Asn Se	r Thr Met Gly S	Pro Pro Ala Asn Ser Thr Met Gly Ser Lys Glu Glu Leu		
	325	330		335		•	515	520	525		
	Arg Leu Val Asn Leu Glu Thr Thr Lys Lys Tyr Ala Pro Val Asp Gly	Thr Thr Lys Lys I	Tyr Ala Pro Val	Asp Gly							
70	340	345	350			70				·	
_	Gly Pro Val Thr Ala Ala Ser Ile Thr Ala Phe Cys His Al	Ser Ile Thr Ale P	Phe Cys His Ala	Le Val Leu		v	<210> 82		٠.		
	355	360	365			v	<211> 505				
•	Asn Gly Gln Val Lys Pro Tyr Leu Leu Ser Gln Glu 11e Pr	Tyr Leu Leu Ser G	3ln Glu 11e Pro	o Pro Asp		v	<212> PRT				
	370	375	380				<213> Homo sapiens	_		•	



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<220>

<210> 83
<211> 374
<212> PRT
<213> Homo sapiens
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<221> Alcohol dehydrogenase beta chain
<222> (1)(374)
<223> Accession No. as of 29 August 2003; P00325
<400> 83
Ser Thr Ala Gly Lys Val Ile Lys Cys Lys Ala Ala Val Leu Trp Glu
5 10 15
Val Lys Lys Pro Phe Ser Ile Glu Asp Val Glu Val Ala Pro Pro Lys
20 25 30
Ala Tyr Glu Val Arg Ile Lys Met Val Ala Val Gly Ile Cys Arg Thr
35 40 . 45
Asp Asp His Val Val Ser Gly Asn Leu Val Thr Pro Leu Pro Val Ile
50 55 60
reu Gly His Glu Ala Ala Gly Ile Val Glu Ser Val Gly Glu Gly Val
70 75 80
Thr Thr Val Lys Pro Gly Asp Lys Val Ile Pro Leu Phe Thr Pro Gln
. S6 06 58
The Alcohol dehydrogenase beta chi (1)(374) Accession No. as of 29 August Accession No. as of 29 August 38 10

Cys Gly Lys Cys Arg Val Cys Lys Asn Pro Glu Ser Asn Tyr Cys Leu

	WO 2004/055519 PCT/RP2003/014057 253/335	WO 2004/055519 PCT/EP2003/014057
	Lys Asn Asp Leu Gly Asn Pro Arg Gly Thr Leu Gln Asp Gly Thr Arg	Pro Met Leu Leu Thr Gly Arg Thr Trp Lys Gly Ala Val Tyr Gly
	115 120 125	305 310 315 320
	Arg Phe Thr Cys Arg Gly Lys Pro Ile His His Phe Leu Gly Thr Ser	Gly Phe Lys Ser Lys Glu Gly Ile Pro Lys Leu Val Ala Asp Phe Met
	130 135 140	325 330 335
	5 Thr Phe Ser Gln Tyr Thr Val Val Asp Glu Asn Ala Val Ala Lys Ile	5 Ala Lys Phe Ser Leu Asp Ala Leu Ile Thr His Val Leu Pro Phe
	145 150 155 160	340 345 350
	Asp Ala Ala Ser Pro Leu Glu Lys Val Cys Leu Ile Gly Cys Gly Phe	Glu Lys Ile Asn Glu Gly Phe Asp Leu Leu His Ser Gly Lys Ser Ile
	165 170 175	355 360 365
	Ser Thr Gly Tyr Gly Ser Ala Val Asn Val Ala Lys Val Thr Pro Gly	Arg Thr Val Leu Thr Phe
	10 180 185 190	10 370
	Ser Thr Cys Ala Val Phe Gly Leu Gly Gly Val Gly Leu Ser Ala Val	
•	195 200 205	
	Met Gly Cys Lys Ala Ala Gly Ala Ala Arg Ile Ile Ala Val Asp Ile	<210> 84
	210 215 220	<211> 241
	15 Asn Lys Asp Lys Phe Ala Lys Ala Lys Glu Leu Gly Ala Thr Glu Cys	15 <212> PRT
	225 230 235 240	<213> Homo sapiens
	ile Asn Pro Gln Asp Tyr Lys Lys Pro ile Gln Glu Val Leu Lys Glu	<220>
	. 245 250 255	<221> Glutathione transferase omega 1
	Met Thr Asp Gly Gly Val Asp Phe Ser Phe Glu Val Ile Gly Arg Leu	<222> (1)(241)
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	Asp Thr Met Met Ala Ser Leu Leu Cys Cys His Glu Ala Cys Gly Thr	<400> 84
	275 280 . 285	
,	Ser Val Ile Val Gly Val Pro Pro Ala Ser Gln Asn Leu Ser Ile Asn	Met Ser Gly Glu Ser Ala Arg Ser Leu Gly Lys Gly Ser Ala Pro Pro
	290 295 300	1 5 10 15
-		
-		

WO 2004/055519 PCT/EP2003/014057 255/335	WO 2004/055519 PCT/EP2003/014057 256/335
Gly Pro Val Pro Glu Gly Ser Ile Arg Ile Tyr Ser Met Arg Phe Cys	Asp Pro Thr Val Ser Ala Leu Leu Thr Ser Glu Lys Asp Trp Gln Gly
. 20 25 30	210 215 220
Pro Phe Ala Glu Arg Thr Arg Leu Val Leu Lys Ala Lys Gly Ile Arg	Phe Leu Glu Leu Tyr Leu Gln Asn Ser Pro Glu Ala Cys Asp Tyr Gly
35 40 45	. 225 230 235 240
His Glu Val Ile Asn Ile Asn Leu Lys Asn Lys Pro Glu Trp Phe Phe	
. 09 22	
Lys Lys Asn Pro Phe Gly Leu Val Pro Val Leu Glu Asn Ser Gln Gly	
65 70 75 80	
Gln Leu Ile Tyr Glu Ser Ala Ile Thr Cys Glu Tyr Leu Asp Glu Ala	<210> 85
85 . 06 . 35	10 <211> 999
Tyr Pro Gly Lys Lys Leu Leu Pro Asp Asp Pro Tyr Glu Lys Ala Cys	<212> PRT
100 105 110	<213> Homo sapiens
Gln Lys Met Ile Leu Glu Leu Phe Ser Lys Val Pro Ser Leu Val Gly	<220>
115 120 125	<221> 150 kDa oxygen-regulated protein precursor (orp150)
Ser Phe ile Arg Ser Gin Asn Lys Glu Asp Tyr Ala Gly Leu Lys Glu	15 <222> (1)(999)
130 135 140	<223> Accession No. as of 29 August 2003: Q9Y4L1
Glu Phe Arg Lys Glu Phe Thr Lys Leu Glu Glu Val Leu Thr Asn Lys	<400> 85
145 150 155 160	
Lys Thr Thr Phe Phe Gly Gly Asn Ser Ile Ser Wet Ile Asp Tyr Leu	Met Ala Asp Lys Val Arg Arg Gln Arg Pro Arg Arg Arg Val Cys Tro
165 170 175	20 1 5 10 15
ile Trp Pro Trp Phe Glu Arg Leu Glu Ala Met Lys Leu Asn Glu Cys	Ala Leu Val Ala Val Leu Leu Ala Ago Leu Leu Ala Leu Ser Ago Thr
180 185 190	20 25 30
Val Asp His Thr Pro Lys Leu Lys Leu Trp Met Ala Ala Met Lys Glu	Leu Ala Val Met Ser Val Asp Leu Gly Ser Glu Ser Met Lys Val Ala
195 200 205	35 40 45

	WO 2004/055519	257/335	PCT/EP2003/014057		WO 2004/055519	PCT/EP2003/0	:P2003/C
	Ile Val Lys Pro Gl	Ile Val Lys Pro Gly Val Pro Met Glu Ile Val	ıl Leu Asn Lys Glu Ser		Thr Ile Val Thr Tyr Gln Met V	Thr Ile Val Thr Tyr Gln Met Val Lys Thr Lys Glu Ala Gly Met Gln	Gln
	50	5.5	09		245	250 . 255	_
	Arg Arg Lys Thr Pro	Arg Arg Lys Thr Pro Val Ile Val Thr Leu Lys	e Glu Asn Glu Arg Phe		Pro Gln beu Gln Ile Arg Gly V	Pro Gln Leu Gln Ile Arg Gly Val Gly Phe Asp Arg Thr Leu Gly Gly	Gly
	65	70 . 75	80		260	265 270	
5		Phe Gly Asp Ser Ala Ala Ser Met Ala Ile Lys	s Asn Pro Lys Ala Thr		5 Leu Glu Met Glu Leu Arg Leu A	Leu Glu Met Glu Leu Arg Leu Arg Glu Arg Leu Ala Gly Leu Phe Asn	Asn
	85	06	ς. 6		275	280 285	
	Leu Arg Tyr Phe Gln	Leu Arg Tyr Phe Gln His Leu Leu Gly Lys Gln	n Ala Asp Asn Pro His		Glu Gln Arg Lys Gly Gln Arg A	Glu Gln Arg Lys Gly Gln Arg Ala Lys Asp Val Arg Glu Asn Pro Arg	Arg
	100	105	110		. 290 295	300	
	Val Ala Leu Tyr Gln	Val Ala Leu Tyr Gln Ala Arg Phe Pro Glu His Glu Leu Thr Phe Asp	s Glu Leu Thr Phe Asp		Ala Met Ala Lys Leu Leu Arg G	Ala Met Ala Lys beu beu Arg Glu Ala Asn Arg beu Lys Thr Val Leu	Leu
2	115	120	125	10	310	315	320
	Pro Gln Arg Gln Thr	Pro Gln Arg Gln Thr Val His Phe Gln Ile Ser Ser Gln Leu Gln Phe	r Ser Gln Leu Gln Phe		Ser Ala Asn Ala Asp His Met A	Ser Ala Asn Ala Asp His Met Ala Gin Ile Giu Gly Leu Wet Asp Asp	ABD
	130	135	140		325	330 335	
	Ser Pro Glu Glu Val	Ser Pro Glu Glu Val Leu Gly Met Val Leu Asn Tyr Ser Arg Ser Leu	n Tyr Ser Arg Ser Leu		Val Asp Phe Lys Ala Lys Val T	Val Asp Phe Lys Ala Lys Val Thr Arg Val Glu Phe Glu Glu Leu Cys	Ş
	145	150 155	160		340	345 350	
51		Ala Glu Asp Phe Ala Glu Gln Pro Ile Lys Asp Ala Val Ile Thr Val	o Ala Val Ile Thr Val	15		Ala Asp Leu Phe Glu Arg Val Pro Gly Pro Val Gln Gln Ala Leu Gln	Gln
	165	170	175		355	360 365	
	Pro Val Phe Phe Asn	Pro Val Phe Phe Asn Gln Ala Glu Arg Arg Ala V	a Val Leu Gln Ala Ala		Ser Ala Glu Met Ser Leu Asp G	Ser Ala Glu Met Ser Leu Asp Glu Ile Glu Gln Val Ile Leu Val Gly	Gly
	180	185	190		370 375	380	
	Arg Met Ala Gly Leu	Arg Met Ala Gly Leu Lys Val Leu Gln Leu Ile Asn Asp Asn Thr	e Asn Asp Asn Thr Ale		Gly Ala Thr Arg Val Pro Arg V	Glỳ Ala Thr Arg Val Pro Arg Val Glu Glu Val Leu Leu Lys Ala Val	Val
20	195	200	205	20	390	395	400
	Thr Ala Leu Ser Tyr	Thr Ala Leu Ser Tyr Gly Val Phe Arg Arg Lys Asp Ile Asn Thr Thr	3 Asp Ile Asn Thr Thr		Gly Lys Glu Glu Leu Gly Lys A	Gly Lys Glu Glu Leu Gly Lys Asn Ile Asn Ala Asp Glu Ala Ala Ala	Ala
	210	215	220		405	410 415	
	Ala Gln Asn Ile Met	Ala Gin Asn ile Met Phe Tyr Asp Met Gly Ser Gly Ser Thr Val	: Gly Ser Thr Val Cys		Met Gly Ala Val Tyr Gln Ala A	Met Gly Ala Val Tyr Gln Ala Ala Ala Leu Ser Lys Ala Phe Lys Val	Val
	225	230 235	240		420	425 430	

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Lys Pro Phe Val	Lys Pro Phe Val Val Arg Asp Ala Val Val Tyr Pro Ile	e Leu Val Glu	Glu Ala Glu Ala Pro Val Glu Asp Gly Ser Gln Pro Pro Pro Pro Glu	er Gln Pro Pro Pro Glu
435	440	445	625 630	635 640
Phe Thr Arg Glu	Phe Thr Arg Glu Val Glu Glu Glu bro Gly 11e H1s Ser	r Leu Lys His	Pro Lys Gly Asp Ala Thr Pro Glu Gly Glu Lys Ala Thr Glu Lys Glu	ilu Lys Ala Thr Glu Lys Glu
450	455 460		645	650 655
5 Asn Lys Arg Val	Asn Lys Arg Val Leu Phe Ser Arg Met Gly Pro Tyr Pro	o Gln Arg Lys	5 Asn Gly Asp Lys Ser Glu Ala Gln Lys Pro Ser Glu Lys Ale Glu Ale	ro Ser Glu Lys Ala Glu Ala
465	470 475	480	999 099.	670
Val Ile Thr Phe	Val Ile Thr Phe Asn Arg Tyr Ser His Asp Phe Asn Phe His Ile Asn	e His Ile Asn	Gly Pro Glu Gly Val Ala Pro Ala Pro Glu Gly Glu Lys Lys Gln Lys	ilu Gly Glu Lys Lys Gln Lys
	485 490	495	675 680	685
Tyr Gly Asp Leu	Tyr Gly Asp Leu Gly Phe Leu Gly Pro Glu Asp Leu Arg Val Phe Gly	g Val Phe Gly	Pro Ala Arg Lys Arg Arg Met Val Glu Glu Ile Gly Val Glu Leu Val	du Ile Gly Val Glu Leu Val
10 500	505	510	. 690 695	700
Ser Gln Asn Leu	Ser Gln Asn Leu Thr Thr Val Lys Leu Lys Gly Val Gly Asp Ser Phe	/ Asp Ser Phe	Val Leu Asp Leu Pro Asp Leu Pro Glu Asp Lys Leu Ala Gln Ser Val	sp Lys Leu Ala Gln Ser Val
515	520 525	10	. 705 710	715 720
Lys Lys Tyr Pro	Lys Lys Tyr Pro Asp Tyr Glu Ser Lys Gly Ile Lys Ala His Phe Asn	a His Phe Asn	Gln Lys Leu Gln Asp Leu Thr Leu Arg Asp Leu Glu Lys Gln Glu Arg	sp Leu Glu Lys Gln Glu Arg
530	535 540		. 725	730 735
15 Leu Asp Glu Ser	Leu Asp Glu Ser Gly Val Leu Ser Leu Asp Arg Val Glu S	Ser Val Phe	15 Glu Lys Ala Ala Asn Ser Leu Glu Ala Phe Ile Phe Glu Thr Gln Asp	he Ile Phe Glu Thr Gln Asp
545	550 . 555		740 745	750
Glu Thr Leu Val	Glu Thr Leu Val Glu Asp Ser Ala Glu Glu Glu Ser Thr L	Leu Thr Lys	Lys Leu Tyr Gln Pro Glu Tyr Gln Glu Val Ser Thr Glu Glu Gln Arg	al Ser Thr Glu Glu Gln Arg
	565 570	575	755 760	765
Leu Gly Asn Thr	Leu Gly Aen Thr Ile Ser Ser Leu Phe Gly Gly Gly Thr Thr Pro Asp		Glu Glu Ile Ser Gly Lys Leu Ser Ala Ala Ser Thr Trp Leu Glu Asp	la Ser Thr Trp Leu Glu Asp
20 580	585	290	20 770 775	780
Ala Lys Glu Asn	Ala Lys Glu Asn Gly Thr Asp Thr Val Gln Glu Glu Glu Glu Ser	Glu Ser Pro	Glu Gly Val Gly Ala Thr Thr Val Met Leu Lys Glu Lys Leu Ala Glu	eu Lys Glu Lys Leu Ala Glu
595	. 600		785	795 800
Ala Glu Gly Ser	Ala Glu Gly Ser Lys Asp Glu Pro Gly Glu Gln Val Glu Leu Lys Glu	Leu Lys Glu	Leu Arg Lys Leu Cys Gln Gly Leu Phe Phe Arg Val Glu Glu Arg Lys	he Arg Val Glu Glu Arg Lys
610	615 620		808	810 815

Lys Trp Pro Glu Arg Leu Ser Ala Leu Asp Asn Leu Leu Asn His Ser	
820 825 830	
Ser Met Phe Leu Lys Gly Ala Arg Leu Ile Pro Glu Met Asp Gln Ile	<210> 86
835 840 845	<211> 271
Phe Thr Glu Val Glu Met Thr Thr Leu Glu Lys Val Ile Asn Glu Thr	5 <212> PRT
. 098 558 058	<213> Homo sapiens
Trp Ala Trp Lys Asn Ala Thr Leu Ala Glu Gln Ala Lys Leu Pro Ala	<2220>
865 870 875 880	<221> Peroxiredoxin 4
Thr Glu Lys Pro Val Leu Leu Ser Lys Asp Ile Glu Ala Lys Met Met	<222> (1) (271)
	10 <223> Accession No. as of 29 August 2003; Q13162
Ala Leu Asp Arg Glu Val Gln Tyr Leu Leu Asn Lys Ala Lys Phe Thr	98 <000>
016 308 006	
Lys Pro Arg Pro Arg Pro Lys Asp Lys Asn Gly Thr Arg Ala Glu Pro	Met Glu Ala Leu Pro Leu Leu Ala Ala Thr Thr Pro Asp His Gly Arg
915 920 925	
Pro Leu Asn Ala Ser Ala Ser Asp Gln Gly Glu Lys Val Ile Pro Pro	15 His Arg Arg Leu Leu Leu Leu Leu Leu Leu Phe Leu Leu Pro Ala
930 935 940	20 25 30
Ala Gly Gln Thr Glu Asp Ala Glu Pro Ile Ser Glu Pro Glu Lys Val	Gly Ala Val Gln Gly Trp Glu Thr Glu Glu Arg Pro Arg Thr Arg Glu
945 950 955 960	35 40 45
Glu Thr Gly Ser Glu Pro Gly Asp Thr Glu Pro Leu Glu Leu Gly Gly .	Glu Glu Cys His Phe Tyr Ale Gly Gln Val Tyr Pro Gly Glu Ala
965 970 975	. 20 50 55 60
Pro Gly Ala Glu Pro Glu Gln Lys Glu Gln Ser Thr Gly Gln Lys Arg	Ser Arg Val Ser Val Ala Asp His Ser Leu His Leu Ser Lys Ala Lys.
066 586 086	65 70 75 80
Pro Leu Lys Asn Asp Glu Leu	Ile Sex Lys Pro Ala Pro Tyr frp Glu Gly Thr Ala Val Ile Asp Gly
	56 06 58

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	Glu Phe Lys Glu Leu Lys Leu Thr Asp Tyr Arg Gly Lys Tyr Leu Val	rg Gly Lys Tyr Leu Val	<210> 87
	100 105		<211> 288
	Phe Phe Phe Tyr Pro Leu Asp Phe Thr Phe Val Cys Pro Thr Glu Ile	al Cys Pro Thr Glu Ile	<212> PRT
	115 120	125	<213> Homo sapiens
40	ile Ala Phe Gly Asp Arg Leu Glu Glu Phe Arg Ser Ile Asn Thr Glu		5 <220>
	130 135	140	<221> MAWD binding protein
	Val Val Ala Cys Ser Val Asp Ser Gln Phe Thr His Le	nr His Leu Ala Trp 11e	<222> (1)(288)
	145 150 1:	. 160	<223> Accession No. as of 29 August 2003: P30039
	Asn Thr Pro Arg Arg Gln Gly Gly Leu Gly Pro ile Arg Ile Pro Leu	o lle Arg Ile Pro Leu	<400> 87
10	165 170	175	
	Leu Ser Asp Leu Thr His Gln Ile Ser Lys Asp Tyr Gly Val Tyr Leu	sp Tyr Gly Val Tyr Leu	Met Lys Leu Pro Ile Phe Ile Ala Asp Ala Phe Thr Ala Arg Ala Phe
	180 185	190	1 5 10 15
	Glu Asp Ser Gly His Thr Leu Arg Gly Leu Phe Ile Ile Asp Asp Lys	e Ile Ile Asp Asp Lys	. Arg Gly Asn Pro Ala Ala Val Cys Leu Leu Glu Asn Glu Leu Asp Glu
	195 200	205	20 25 30
15	Gly ile Leu Arg Gln ile Thr Leu Asn Asp Leu Pro Val	nu Pro Val Gly Arg Ser	Asp Met His Gln Lys Ile Ala Arg Glu Met Asn Leu Ser Glu Thr Ala
	210 215	220	35 40 45
	Val Asp Glu Thr Leu Arg Leu Val Gln Ala Phe Gln Tyr	e Gln Tyr Thr Asp Lys	Phe Ile Arg Lys Leu His Pro Thr Asp Asn Phe Ala Gln Ser Ser Cys
	225 230 235	5 240	29 99 99
•	His Gly Glu Val Cys Pro Ala Gly Trp Lys Pro Gly Ser	o Gly Ser Glu Thr 11e	Phe Gly Leu Arg Trp Phe Thr Pro Ala Ser Glu Val Pro Leu Cys Gly
20	245 250	255	65 70 75 80
	Ile Pro Asp Pro Ala Gly Lys Leu Lys Tyr Phe Asp Lys	e Asp Lys Leu Asn	His Ala Thr Leu Ala Ser Ala Ala Val Leu Phe His Lys Ile Lys Asn
	260 265		56. 06 58
			Met Asn Ser Thr Leu Thr Phe Val Thr Leu Ser Gly Glu Leu Arg Ala

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			200/353
	Arg Arg Ala Glu Asp Gly I.	Arg Arg Ala Glu Asp Gly Ile Val Leu Asp Leu Pro Leu Tyr Pro Ala	<210> 88
	115	. 120 . 125	<211> 511
	His Pro Gln Asp Phe His Gi	His Pro Gin Asp Phe His Glu Val Glu Asp Leu Ile Lys Thr Ala Ile	<212> PRT
	130	135 140	<213> Homo saplens
50	5 Gly Asn Thr Leu Val Gln As	Gly Asn Thr Leu Val Gln Asp Ile Cys Tyr Ser Pro Asp Thr Gln Lys	5 <220>
	145 150	155. 160	<221> Alpha-amylase 2B precursor
	Leu Leu Val Arg Leu Ser Asp Val Tyr Asn Arg Ser Pl	ip Val Tyr Asn Arg Ser Phe Leu Glu Asn	<222> (1)(511)
	165	170 175	<223> Accession No. as of 29 August 2003: P19961
•		Leu Lys Val Asn Thr Glu Asn Leu Leu Gln Val Glu Asn Thr Gly Lys	<400> 88
21	180	185 190	
	Val Lys Gly Leu Ile Leu Th	Val Lys Gly Leu Ile Leu Thr Leu Lys Gly Glu Pro Gly Gly Gln Thr	Met Lys Phe Phe Leu Leu Phe Thr Ile Gly Phe Cys Trp Ala Gln
	195	200 205	1 5 10 15
•	Gln Ala Phe Asp Phe Tyr Se	Gin Ala Phe Asp Phe Tyr Ser Arg Tyr Phe Ala Pro Trp Val Gly Vel	Tyr Ser Pro Asn Thr Gin Gin Gly Arg Thr Ser Ile Val His Leu Phe
	210 215	5 220	20 25 30
15		Ala Glu Asp Pro Val Thr Gly Ser Ala His Ala Val Leu Ser Ser Tyr	15 Glu Trp Arg Trp Val Asp Ile Ala Leu Glu Cys Glu Arg Tyr Leu Ala
	225 230	235 240	35 40 45
	Trp Ser Gin His Leu Gly Lys Lys Glu Met His Ala Ph	s Lys Glu Met His Ala Phe Gln Cys Ser	Pro Lys Gly Phe Gly Gly Val Gln Val Ser Pro Asn Glu Asn Val
	245	250 255	. 55 60
	His Arg Gly Gly Glu Leu Gl	His Arg Gly Gly Glu Leu Gly Ile Sex Leu Arg Pro Asp Gly Arg Val	Ala ile His Asn Pro Phe Arg Pro Trp Trp Glu Arg Tyr Gln Pro Val
8	260	. 265 270	20 65 70 75 80
	Asp Ile Arg Gly Gly Ala Al	Asp Ile Arg Gly Gly Ala Ala Val Val Leu Glu Gly Thr Leu Thr Ala	Ser Tyr Lys Leu Cys Thr Arg Ser Gly Asn Glu Asp Glu Phe Arg Asn
	275	280 285	56 06 58
			. Met Val Thr Arg Cys Asn Asn Val Gly Val Arg Ile Tyr Val Asp Ala

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Val Ile Asn His Met Ser Gly Asn Ala Val Ser Ala Gly Thr Ser Ser	Asp Arg Ale Leu Val Phe Val Asp Asn His Asp Asn Gln Arg Gly His
115 120 125	305 310 315 320
Thr Cys Gly Ser Tyr Phe Asn Pro Gly Ser Arg Asp Phe Pro Ala Val	Gly Ala Gly Gly Ala Ser Ile Leu Thr Phe Trp Asp Ala Arg Leu Tyr
130 . 135 140	325 330 335
5 Pro Tyr Ser Gly Trp Asp Phe Asn Asp Gly Lys Cys Lys Thr Gly Ser	5 Lys Met Ala Val Gly Phe Met Leu Ala His Pro Tyr Gly Phe Thr Arg
145 150 155 160	340 345 350
Gly Asp Ile Glu Asn Tyr Asn Asp Ala Thr Gln Val Arg Asp Cys Arg	Val Met Ser Ser Tyr Arg Trp Pro Arg Gln Phe Gln Asn Gly Asn Asp
165 170 175	355 360 365
Leu Val Gly Leu Leu Asp Leu Ala Leu Glu Lys Asp Tyr Val Arg Ser	Val Asn Asp Trp Val Gly Pro Pro Asn Asn Asn Gly Val Ile Lys Glu
10 180 185 190	10 370 375 380
Lys Ile Ala Glu Tyr Met Asn His Leu Ile Asp Ile Gly Val Ala Gly	Val Thr Ile Asn Pro Asp Thr Thr Cys Gly Asn Asp Trp Val Cys Glu
195 200 205	385 390 395 400
Phe Arg Leu Asp Ala Ser Lys His Met Trp Pro Gly Asp Ile Lys Ala	His Arg Trp Arg Gln Ile Arg Asn Met Val Asn Phe Arg Asn Val Val
210 215 220	405 410 415
15 Ile Leu Asp Lys Leu His Asn Leu Asn Ser Asn Trp Phe Pro Ala Gly	15 Asp Gly Gln Pro Phe Thr Asn Trp Tyr Asp Asn Gly Ser Asn Gln Val
225 230 ,235 240	420 425 430
Ser Lys Pro Phe Ile Tyr Gln Glu Val Ile Asp Leu Gly Gly Glu Pro	Ala Phe Gly Arg Gly Asn Arg Gly Phe Ile Vel Phe Asn Asn Asp Asp
245 250 255	435 440 445
Ile Lys Ser Ser Asp Tyr Phe Gly Asn Gly Arg Val Thr Glu Phe Lys	Trp Thr Phe Ser Leu Thr Leu Gln Thr Gly Leu Pro Ala Gly Thr Tyr
20 260 265 270	20 450 455 460
Tyr Gly Ala Lys Leu Gly Thr Val Ile Arg Lys Trp Asn Gly Glu Lys	Cys Asp Val 11e Ser Gly Asp Lys 11e Asn Gly Asn Cys Thr Gly 11e
275 280 285	465 470 475 480
Met Ser Tyr Leu Lys Asn Trp Gly Glu Gly Trp Gly Phe Met Pro Ser	Lys Ile Tyr Val Ser Asp Asp Gly Lys Ala His Phe Ser Ile Ser Asn
290 295 300	485 490 495

3/014057		·																٠			
PCT/EP2003/014057	ıla Glu Ser Lys Leu	510								P04746		y Phe Cys Trp Ala Gln	15	r Ile Val His Leu Phe	30	Glu Arg Tyr Leu Ala	45	Pro Asn Glu Asn Val	09	Arg Tyr Gln Pro Val	08
269/335	Ser Ala Glu Asp Pro Phe Ile Ala Ile His Ala Glu Ser Lys Leu	505						Alpha-amylase, pancreatic precursor		Accession No. as of 29 August 2003; P04746		Met Lys Phe Phe Leu Leu Leu Phe Thr Ile Gly Phe Cys Trp Ala Gln	10	Tyr Ser Pro Asn Thr Gln Gln Gly Arg Thr Ser 11e Val His Leu Phe	25	Glu Trp Arg Trp Val Asp Ile Ala Leu Glu Cys Glu Arg Tyr Leu Ala	40	Pro Lys Gly Phe Gly Gly Val Gln Val Ser Pro Pro Asn Glu Asn Val	55	Ala ile Tyr Asn Pro Phe Arg Pro Trp Trp Glu Arg Tyr Gln Pro Val	75
WO 2004/055519	Ser Ala Glu Asp Pro	200	<210> 89	<211> 511	<212> PRT	<213> Homo sapiens	<220>	<221> Alpha-amylase	<222> (1)(511)	<223> Accession No.	<400>	Met Lys Phe Phe Leu I	1 5	lyr Ser Pro Asn Thr G	20	ilu Trp Arg Trp Val A	35	ro Lys Gly Phe Gly G	90	la ile Tyr Asn Pro Pl	65 70

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Ser Tyr Lys Leu Cys Thr Arg Ser Gly Asn Glu Asp Glu Phe Arg Asn

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Met Val Thr Arg Cys Asn Asn Val Gly Val Arg Ile Tyr Val Asp Ala

5 Val Ile Asn His Met Cys Gly Asn Ala Val Ser Ala Gly Thr Ser Ser

Thr Cys Gly Ser Tyr Phe Asn Pro Gly Ser Arg Asp Phe Pro Ala Val

Pro Tyr Ser Gly Trp Asp Phe Asn Asp Gly Lys Cys Lys Thr Gly Ser

Gly Asp Ile Glu Asn Tyr Asn Asp Ala Thr Gln Val Arg Asp Cys Arg

10 145

Leu Thr Gly Leu Leu Asp Leu Ala Leu Glu Lys Asp Tyr Val Arg Ser

15 Lys ile Ala Glu Tyr Met Asn His Leu ile Asp ile Gly Val Ala Gly

Phe Arg Leu Asp Ala Ser Lys His Met Trp Pro Gly Asp Ile Lys Ala

Ile Leu Asp Lys Leu His Asn Leu Asn Ser Asn Trp Phe Pro Ala Gly

Ser Lys Pro Phe Ile Tyr Gln Glu Val Ile Asp Leu Gly Gly Glu Pro

20 225

ile Lys Ser Ser Asp Tyr Phe Gly Asn Gly Arg Val Thr Glu Phe Lys

WO 2004/055519	PCT/E	PCT/EP2003/014057	Š	WO 2004/055519		DCT/F02003/044047
			•		272/335	1.C.1.Ef 2003/01403/
Tyr Gly Ale Lys Leu Gly Thr Val Ile Arg Lys Trp Asn	rg Lys Trp Asn Gly Glu Lys	Lys	Ĭ	Cys Asp Val Ile Ser Gly Asp Lys Ile Asn Gly Asn Cys Thr Gly Ile	Ile Asn Gly Asn Cys T	hr Gly Ile
275 280	285			465	475	480
Met Ser Tyr Leu Lys Asn Trp Gly Glu Gly Trp Gly Phe	ly Trp Gly Phe Val Pro Ser	Ser	~	Lys ile Tyr Val Ser Asp Asp Gly Lys Ala His Phe Ser Ile Ser Asn	Lys Ala His Phe Ser I	le Ser Agn
290 295	300			. 485	490	495
5 Asp Arg Ala Leu Val Phe Val Asp Asn His Asp Asn Gln	ls Asp Asn Gln Arg Gly His	His	'n	Ser Ala Glu Asp Pro Phe Ile Ala Ile His Ala Glu Ser Lys Leu	Ile His Ala Glu Ser L	ys Leu
305 310	315	320		200	505	510
Gly Ala Gly Gly Ala Ser Ile Leu Thr Phe Trp'Asp Ala	oe Trp'Asp Ala Arg Leu Tyr	Tyr				
325 330	335					
Lys Met Ala Val Gly Phe Met Leu Ala His Pro Tyr Gly	s Pro Tyr Gly Phe Thr Arg	Arg	·	<210> 90		
10 340 345	350		01	<211> 553		
Val Met Ser Ser Tyr Arg Trp Pro Arg Gln Phe Gln Asn	n Phe Gln Asn Gly Asn Asp	Asp	·	<212> PRT		-
355 360	365		·	<213> Homo sapiens		
Val Asn Asp Trp Val Gly Pro Pro Asn Asn Asn Gly Val	n Asn Gly Val Ile Lys Glu	glu	•	<220>		
370 375.	380		•	<221> ATP synthase alpha chain		
15 Val Thr Ile Asn Pro Asp Thr Thr Cys Gly Asn Asp Trp	y Asn Asp Trp Val Cys Glu	Glu .	. 51	<222> (1)(553)		
385 390	395	400		<223> Accession No. as of 29 August 2003; P25705	ugust 2003: P25705	٠.
His Arg Trp. Arg Gln Ile Arg Asn Met Val Ile Phe Arg	l Ile Phe Arg Asn Val Val	Val		<400> 90		
405 410	0 415			·	•	
Asp Gly Gln Pro Phe Thr Asn Trp Tyr Asp Asn Gly	p Asn Gly Ser Asn Gln Val	Val	~	Met Leu Ser Val Arg Val Ala Ala Ala Val Val Arg Ala Leu Pro Arg	Ala Val Val Arg Ala L	au Pro Arg
20 420 425	430		20 1	ហ	10	15
Ala Phe Gly Arg Gly Asn Arg Gly Phe Ile Val Phe Asn	e Val Phe Asn Asn Asp Asp	Авр	•	Arg Ala Gly Leu Val Ser Arg Asn Ala Leu Gly Ser Ser Phe Ile Ala	Ala Leu Gly Ser Ser P	ne Ile Ala
435 440	445			20	25 30	
Trp Ser Phe Ser Leu Thr Leu Gln Thr Gly Leu Pro Ala Gly Thr Tyr	Y Leu Pro Ala Gly Thr	Tyr		Ala Arg Asn Phe His Ala Ser Asn Thr His Leu Gin Lys Thr Gly Thr	Thr His Leu Gln Lys T	ır Gly Thr
450 455	460			35 40	. 45	

	WO 2004/055519 PCT/EP2003/014057 273/335	WO 2004/055519 274/335
	Ale Glu Met Ser Ile Leu Glu Glu Arg Ile Leu Gly Ala Asp Thr	Lys Leu Tyr Cys Ile Tyr Val Ala Ile Gly Gln Lys Arg Ser Thr Val
	50 55 60	245 250 255
	Ser Val Asp Leu Glu Thr Gly Arg Val Leu Ser Ile Gly Asp Gly	Ala Gin Leu Val Lys Arg Leu Thr Asp Ala Asp Ala Met Lys Tyr Thr
	65 70 75 80	260 265 270
	5 Ile Ala Arg Val His Gly Leu Arg Asn Val Gln Ala Glu Glu Met Val	5 Ile Val Val Ser Ala Thr Ala Ser Amp Ala Ala Pro Leu Gln Tyr Leu
	85 90 95	275 280 285
	Glu Phe Ser Gly Leu Lys Gly Met Ser Leu Asn Leu Glu Pro Asp	Ala Pro Tyr Ser Gly Cys Ser Met Gly Glu Tyr Phe Arg Asp Asn Gly
	100 105 110	290 295 300
	Asn Val Gly Val Val Val Phe Gly Asn Asp Lys Leu Ile Lys Glu Gly	Lys His Ala Leu Ile Tyr Asp Asp Leu Ser Lys Gln Ala Val Ala
	10 115 120 125	10 305 310 315 320
	Asp Ile Val Lys Arg Thr Gly Ala Ile Val Asp Val Pro Val Gly Glu	Tyr Arg Gln Met Ser Leu Leu Arg Arg Pro Pro Gly Arg Glu Ala
	130 135 140	325 330 335
	Glu Leu Leu Gly Arg Val Val Asp Ala Leu Gly Asn Ala Ile Asp Gly	Tyr Pro Gly Asp Val Phe Tyr Leu His Ser Arg Leu Leu Glu Arg Ala
	145 150 155 160	340 345 350
	15 Lys Gly Pro Ile Gly Ser Lys Thr Arg Arg Val Gly Leu Lys Ala	15 Ala Lys Met Asn Asp Ala Phe Gly Gly Ger Leu Thr Ala Leu Pro
	165 170 175	355 360 365
	Pro Gly 11e 11e Pro Arg 11e Ser Val Arg Glu Pro Met Gln Thr Gly	Val 11e Glu Thr Gln Ala Gly Asp Val Ser Ala Tyr 11e Pro Thr Asn
	180 185 190	370 375 380
	Ile Lys Ala Val Asp Ser Leu Val Pro Ile Gly Arg Gly Gln Arg Glu	Val ile Ser ile Thr Asp Gly Gln ile Phe Leu Glu Thr Glu Leu Phe
, -	20 195 200 205	20 385 390 395 400
	Leu ile ile Gly Asp Arg Gln Thr Gly Lys Thr Ser ile Ala ile Asp	Tyr Lys Gly ile Arg Pro Ala ile Asn Val Gly Leu Ser Val Ser Arg
	210 215 220	405 410
	Thr ile ile Asn Gln Lys Arg Phe Asn Asp Gly Ser Asp Glu Lys Lys	Val Gly Ser Ala Ala Gln Thr Arg Ala Met Lys Gln Val Ala Gly Thr
	225 230 235 240	420 425 430
·		
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Met Lys Leu Glu Leu Ala Gln Tyr Arg Glu Val Ala Ala Phe Ala Gln	<222> (1) (742)
435 440 445	<223> Accession No. as of 29 August 2003; P19835
Phe Gly Ser Asp Leu Asp Ala Ala Thr Gln Gln Leu Leu Ser Arg Gly	<400> 91
450 455 460	
5 Val Arg Leu Thr Glu Leu Leu Lys Gln Gly Gln Tyr Ser Pro Met Ala	5 Met Gly Arg Leu Gln Leu Val Val Leu Gly Leu Thr Cys Cys Trp Ala
465 470 475 480	1 5 10 15
ile Glu Glu Gln Val Ala Val ile Tyr Ala Gly Val Arg Gly Tyr Leu	Val Ala Ser Ala Ala Lys Leu Gly Ala Val Tyr Thr Glu Gly Gly Phe
485 490 495	20 25 30
Asp Lys Leu Glu Pro Ser Lys Ile Thr Lys Phe Glu Asn Ala Phe Leu	Val Glu Gly Val Asn Lys Lys Leu Gly Leu Gly Asp Ser Val Asp
10 500 505 510	10 35 40 45
Ser His Val Val Ser Gln His Gln Ala Leu Leu Gly Thr Ile Arg Ala	Ile Phe Lys Gly Ile Pro Phe Ala Ala Pro Thr Lys Ala Leu Glu Asn
515 520 525	95 55 60
Asp Gly Lys Ile Ser Glu Gln Ser Asp Ala Lys Leu Lys Glu Ile Val	Pro Gin Pro His Pro Gly Trp Gin Gly Thr Leu Lys Ala Lys Asn Phe
530 535 540	65 70 75 80
15 Thr Asn Phe Leu Ala Gly Phe Glu Ala	15 Lys Lys Arg Cys Leu Gln Ala Thr Ile Thr Gln Asp Ser Thr Tyr Gly
545 550	56 06 58
	Asp Glu Asp Cys Leu Tyr Leu Asn Ile Trp Val Pro Gln Gly Arg Lys
	100 105 110
<210> 91	Gin Val Ser Arg Asp Leu Pro Val Met Ile Trp Ile Tyr Gly Gly Ala
20 <211> 742	20 115 120 125
<212> PRT	Phe Leu Met Gly Ser Gly His Gly Ala Asn Phe Leu Asn Asn Tyr Leu
<213> Homo sapiens	130 135 140
<220>	Tyr Asp Gly Glu Glu ile Ala Thr Arg Gly Asn Val ile Val Thr

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Phe Asn Tyr Arg Val Gly Pro Leu Gly Phe Leu Ser Thr Gly Asp Ala	Asn Lys Gly Asn Lys
165 170 175	355
Asn Leu Pro Gly Asn Tyr Gly Leu Arg Asp Gln His Met Ala Ile Ala	Ser Glu Phe Thr Ile
180 185 190	370
o Trp Val Lys Arg Asn Ile Ala Ala Phe Gly Gly Asp Pro Asn Asn Ile	5 Asp Val Tyr Thr Glu
200 , 205	385
Thr Leu Phe Gly Glu Ser Ala Gly Gly Ala Ser Val Ser Leu Gin Thr	Lys Lys Thr Val Val
210 215 220	405
Leu Ser Pro Tyr Asn Lys Gly Leu lle Arg Arg Ala lle Ser Gln Ser	Thr Glu Ile Ala Leu
225 230 235 240	10 420
Gly Val Ala Leu Ser Pro Trp Val Ile Gln Lys Asn Pro Leu Phe Trp	Thr Tyr Ala Tyr Leu
245 250 255	435
Ala Lys Lys Val Ala Glu Lys Val Gly Cys Pro Val Gly Asp Ala Ala	Lys Trp Val Gly Ala
260 265 270 .	450
Arg Met Ala Gin Cys Leu Lys Val Thr Asp Pro Arg Ala Leu Thr Leu	15 Lys Pro Phe Ala Thr
275 280 285	465
Ala Tyr Lys Val Pro Leu Ala Gly Leu Glu Tyr Pro Met Leu His Tyr	Ser Lys Ala Met Ile
290 295 300	485
Val Gly Phe Val Pro Val Ile Asp Gly Asp Phe Ile Pro Ala Asp Pro	Pro Asn Met Gly Asp 5
305 310 315 320	20 500
ile Asn Leu Tyr Ala Asn Ala Asp Ile Asp Tyr ile Ala Gly Thr	Thr Glu Asn Ser Gly 1
325 330 335	515
Asn Asn Met Asp Gly His Ile Phe Ala Ser Ile Asp Met Pro Ala Ile	Ser Met Lys Arg Ser I
340 345 350	530

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Lys Val Thr Glu Glu Asp Phe Tyr Lys Leu Val

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Thr Lys Gly Leu Arg Gly Ala Lys Thr Thr Phe

Ser Trp Ala Gin Asp Pro Ser Gin Glu Asn Lys

Asp Phe Glu Thr Asp Val Leu Phe Leu Val Pro

Ala Gln His Arg Ala Asn Ala Lys Ser Ala Lys

Phe Ser His Pro Ser Arg Met Pro Val Tyr Pro

Asp His Ala Asp Asp Ile Gln Tyr Val Phe Gly

Pro Thr Gly Tyr Arg Pro Gln Amp Arg Thr Val

Ala Tyr Trp Thr Asn Phe Ala Lys Thr Gly Asp

Ser Ala Val Pro Thr His Trp Glu Pro Tyr Thr

Tyr Leu Glu Ile Thr Lys Lys Met Gly Ser Ser

Leu Arg Thr Asn Phe Leu Arg Tyr Trp Thr Leu

WO 2004/055519 PCT/EP2003/014057 280/335	Pro Ala Val Ile Arg Phe	740			5 <210> 92	<211> 467	<212> PRT	<213> Homo sapiens	<220>	10 <221> Pancreatic lipase related protein precursor	<222> (1)(467)	<223> Accession No. as of 29 August 2003; P54315	<400> 92		15 Met Leu Ile Phe Trp Thr Ile Thr Leu Phe Leu Leu Gly Ala Ala Lys	1 5 10 15	Gly Lys Glu Val Cys Tyr Glu Asp Leu Gly Cys Phe Ser Asp Thr Glu	20 25 30	Pro Trp Gly Gly Thr Ala 11e Arg Pro Leu Lys 11e Leu Pro Trp Ser	20 35 40 45	Pro Glu Lys 11e Gly Thr Arg Phe Leu Leu Tyr Thr Asn Glu Asn Pro		Asn Asn Phe Gln Ile Leu Leu Ser Asp Pro Ser Thr Ile Glu Ala	. 75 80
WO 2004/055519 PCT/EP2003/014057 279/335	Thr Tyr Leu Ala Leu Pro Thr Val Thr App Gln Glu Ala Thr Pro Val	545 550 555 560.	Pro Pro Thr Gly Asp Ser Glu Ala Thr Pro Val Pro Pro Thr Gly Asp	565 570 575	5 Ser Glu Thr Ala Pro Val Pro Pro Thr Gly Asp Ser Gly Ala Pro Pro	585 590	Gly Asp Ser Gly Ala Pro Pro Val	509 009 565	Asp Ser Gly Ala Pro Pro Val Pro Pro Thr Gly Asp Ser Gly Ala Pro	10 610 615 620	Pro Val Pro Pro Thr Gly Asp Ser Gly Ala Pro Pro Val Pro Pro Thr	625 630 635 640	val P	059	15 Pro Pro Val Pro Pro Thr Gly Asp Ala Gly Pro Pro Pro Val Pro Pro	660 665 670	Thr Gly Asp Ser Gly Ala Pro Pro Val Pro Pro Thr Gly Asp Ser Gly	675 680 685	Ala Pro Pro Val Thr Pro Thr Gly Asp Ser Glu Thr Ala Pro Val Pro	20 690 695 700	Pro Thr Gly Asp Ser Gly Ala Pro Pro Val Pro Pro Thr Gly Asp Ser	705 710 715 720	Glu Ala Ala Pro Val Pro Pro Thr Asp Asp Ser Lys Glu Ala Gln Met	725 730 735

WO 2004/055519 PCT/EP2003/014057 281/335	WO 2004/055519 PCT/EP2003/0140
Ser Asn Phe Gln Met Asp Arg Lys Thr Arg Phe 11e 11e His Gly Phe	Thr Arg Asp Phe Val Ala Cys Asn His Leu Arg Ser Tyr Lys Tyr Tyr
	275 280 285
ile Asp Lys Gly Asp Glu Ser Trp Val Thr Asp Met Cys Lys Lys Leu	Leu Glu Ser Ile Leu Asn Pro Asp Gly Phe Ala Ala Tyr Pro Cys Thr
100 105 110	290 295 300 ·
. Phe Glu Val Glu Glu Val Asn Cys Ile Cys Val Asp Trp Lys Lys Gly	5 Ser Tyr Lys Ser Phe Glu Ser Asp Lys Cys Phe Pro Cys Pro Asp Gln
115 120 125	305 310 315 320
Ser Gln Ala Thr Tyr Thr Gln Ala Ala Asn Asn Val Arg Val Val Gly	Gly Cys Pro Gln Met Gly His Tyr Ala Asp Lys Phe Ala Gly Arg Thr
130 135 140	325 330 335
Ala Gln Val Ala Gln Met Leu Asp Ile Leu Thr Glu Tyr Ser Tyr	Ser Glu Glu Gln Gln Lys Phe Phe Leu Asn Thr Gly Glu Ala Ser Asn
145 150 155 160	10 340 345 350
Pro Pro Ser Lys Val His Leu Ile Gly His Ser Leu Gly Ala His Val	Phe Ala Arg Trp Arg Tyr Gly Val Ser Ile Thr Leu Ser Gly Arg Thr
165 170 175	355 360 365
Ala Gly Glu Ala Gly Ser Lys Thr Pro Gly Leu Ser Arg Ile Thr Gly	Ala Thr Gly Gln 11e Lys Val Ala Leu Phe Gly Asn Lys Gly Asn Thr
180 185 190	370 375 380
Leu Asp Pro Val Glu Ala Ser Phe Glu Ser Thr Pro Glu Glu Val Arg	15 His Gln Tyr Ser Ile Phe Arg Gly Ile Leu Lys Pro Gly Ser Thr His
200 205	385 390 395 400
Leu Asp Pro Ser Asp Ala Asp Phe Val Asp Val Ile His Thr Asp Ala	Ser Tyr Glu Phe Asp Ala Lys Leu Asp Val Gly Thr Ile Glu Lys Val
210 215 220	405 410 415
Ala Pro Leu Ile Pro Phe Leu Gly Phe Gly Thr Asn Gln Gln Met Gly	Lys Phe Leu Trp Asn Asn Asn Val Ile Asn Pro Thr Leu Pro Lys Val
225 230 235 240	20 420 425 430
His Leu Asp Phe Phe Pro Asn Gly Gly Glu Ser Met Pro Gly Cys Lys	Gly Ale Thr Lys Ile Thr Val Gln Lys Gly Glu Glu Lys Thr Val Tyr
245 .250 .255	435 440 445
Lys Asn Ala Leu Ser Gin ile Val Asp Leu Asp Gly ile Trp Ala Gly	Asn Phe Cys Ser Glu Asp Thr Val Arg Glu Asp Thr Leu Leu Thr Leu
260 265 270	450 . 455 460

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	14057																									•	
	PCT/EP2003/014057	e Ile His Gly Phe	95	t Cys Lys Lys Met	110	p Trp Arg His Gly	125	e Arg Val Val Gly		r Gln Leu Gly Tyr	160	u Gly Ala His Thr	175	l Gly Arg Ile Thr	190	u Pro Glu Glu Val	205	l ile His Thr Asp		: Ser Gln Lys Val	240	ı Met Pro Gly Cya	255	Gly Ile Trp Glu	270		
	284/335	g Lys Thr Arg Phe Il	90	ir Trp Pro Ser Asp Me	105	n Cys Ile Cys Val As	120	n Ala Val Gin Agn Il	5 140	e Gln Ala Leu Ser Th	155	l Ile Gly His Ser Lev	170	g Leu Gly Gly Arg Va	185	o Cys Phe Gln Asp Glu	200	a Val Phe Val Asp Val	5 220	r Leu Gly Phe Gly Met	235	o Asn Gly Gly Lys Glı	250	r ile Thr Asp ile Asp	265		
	WO 2004/055519	Ser Asn Phe Gln Leu Asp Arg Lys Thr Arg Phe 11e 11e His Gly Phe	85	Asp Lys Ala Glu Asp Ser Trp Pro Ser Asp Met Cys Lys Lys Met	100	Phe Glu Val Glu Lys Val Asn Cys Ile Cys Val Asp Trp Arg His Gly	115	Ser Arg Ala Met Tyr Thr Gln Ala Vel Gln Aen Ile Arg Vel Val Gly	130 135	Ala Glu Thr Ala Phe Leu Ile Gln Ala Leu Ser Thr Gln Leu Gly Tyr	150	Sor Leu Glu Asp Val His Val Ile Gly His Ser Leu Gly Ala His Thr	165	Ala Ala Glu Ala Gly Arg Arg Leu Gly Gly Arg Val Gly Arg Ile Thr	180	Gly Leu Asp Pro Ala Gly Pro Cys Phe Gln Asp Glu Pro Glu Glu Val	195	Arg Leu Asp Pro Ser Asp Ala Val Phe Val Asp Val Ile His Thr Asp	210 215	Ser Ser Pro Ile Val Pro Ser Leu Gly Phe Gly Met Ser Gln Lys Val	230	Gly His Leu Asp Phe Phe Pro Asn Gly Gly Lys Glu Met Pro Gly Cys	245	Lys Lys Asn Val Leu Ser Thr Ile Thr Asp Ile Asp Gly Ile Trp Glu	260		٠.
	W0 2	Ser		печ		5 Phe		Ser		Ala	10 145	Ser		Ala		15 Gly		Arg		Ser	20 225	Gly	-	Lys			
															-												
	PCT/EP2003/014057					*					эсиквог		1317			ou Ala Thr Val Arg	. 15	ie Ser Asp Glu Lys	30	u Leu Pro Trp Ser	45	r Asn Glu Asn Pro		p Thr 11e Glu Ala			•
	283/335										Pancreatic lipase related protein 2 precursor		Accession No. as of 29 August 2003; P54317			15 Met Leu Pro Pro Trp Thr Leu Gly Leu Leu Leu Leu Ala	10	Gly Lys Glu Val Cys Tyr Gly Gln Leu Gly Cys Phe Ser	25	Pro Trp Ala Gly Thr Leu Gln Arg Pro Val Lys Leu Leu		Pro Glu Asp Ile Asp Thr Arg Phe Leu Leu Tyr Thr Asn	55	Asn Asn Phe Gln Leu Ile Thr Gly Thr Glu Pro Asp Thr	70 75		
·	WO 2004/055519	Thr Pro Cys	465			5 <210> 93	<211> 469	<212> PRT	<213> Homo sapiens	<220>	10 <221> Pancreatic 1	<222> (1)(469)	<223> Accession No	<400> 93		15 Met Leu Pro Pro Trp	1 2	Gly Lys Glu Val Cys	. 50	Pro Trp Ala Gly Thr	20 35	Pro Glu Asp Ile Asp	50	Asn Asn Phe Gln Leu	65		

	WO 2004/055519 285/335	PCT/EP2003/014057	WO 2004/055519 Pd 286/335	PCT/EP2003/014057
	Gly Ile Gly Gly Phe Val Ser Cys Asn His Leu Arg Ser	Leu Arg Ser Phe Glu Tyr	Ser Leu Tyr Pro Cys	
	275 280	285	465	
	Tyr Ser Ser Val Leu Aan Pro Asp Gly Phe Leu Gly	Phe Leu Gly Tyr Pro Cys		
	290 . 295	300		
ıc	Ala Ser Tyr Asp Glu Phe Gln Glu Ser Lys Cys Phe Pro	Cys Phe Pro Cys Pro Ala	5 <210> 94.	
	305. 310	315 320	<211> 465	
	Glu Gly Cys Pro Lys Met Gly His Tyr Ala Asp Gln Phe	Asp Gln Phe Lys Gly Lys	<212> PRT	
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01	340 345	350	10 <221> Triacylglycerol lipase, pancreatic precursor	
	Asn Phe Thr Ser Trp Arg Tyr Lys Val Ser Val Thr Leu	Val Thr Leu Ser Gly Lys	<222> (1)(465)	
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	370 375	086		
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	385 390	395 400	1 5 10	15
	Ser His Thr Cys Ala Ile Asp Val Asp Phe Asn Val Gly	Asn Val Gly Lys Ile Gln	Lys Glu Val Cys Tyr Glu Arg Leu Gly Cys Phe Ser Asp Asp Ser Pro	Ser Pro
	405 410	415	20 25 30	
	Lys Val Lys Phe Leu Trp Asn Lys Arg Gly 11e Asn Leu Ser Glu Pro	ile Asn Leu Ser Glu Pro	Trp Ser Gly Ile Thr Glu Arg Pro Leu His Ile Leu Pro Trp Ser Pro	Ser Pro
20	420 425	430 20	0 35 40 45	
	Lys Leu Gly Ala Ser Gin Ile Thr Val Gin Ser Gly Glu Asp Gly Thr	Ser Gly Glu Asp Gly Thr	Lys Asp Val Asn Thr Arg Phe Leu Leu Tyr Thr Asn Glu Asn Pro Asn	Pro Asn
	435 440	445	. 55 60	
	Glu Tyr Aen Phe Cys Ser Ser Asp Thr Val Glu Glu Asn Val Leu Gln	Glu Glu Asn Val neu Gln	Asn Phe Gln Glu Val Ala Ala Asp Ser Ser Ser Ile Ser Gly Ser Asn	Ser Asn
	450 455		65 70 75	80

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Phe Lys Thr Asn Arg Lys Thr Arg phe Ile Ile His Gly Phe Ile Asp	Arg Asp Phe Ale Ale Cys Asn His Leu Arg Ser Tyr Lys Tyr Thr
85 . 90	275 280 285
Lys Gly Glu Glu Asn Trp Leu Ala Asn Val Cys Lys Asn Leu Phe Lys	Asp Ser Ile Val Asn Pro Asp Gly Phe Ala Gly Phe Pro Cys Ala Ser
100 105 110	290 295 300
Val Glu Ser Val Asn Cys Ile Cys Val Asp Trp Lys Gly Gly Ser Arg	5 Tyr Asn Val Phe Thr Ala Asn Lys Cys Phe Pro Cys Pro Ser Gly Gly
115 120 125	305 310 315 320
Thr Gly Tyr Thr Gln Ala Ser Gln Asn Ile Arg Ile Val Gly Ala Glu	Cys Pro Gln Met Gly His Tyr Als Asp Arg Tyr Pro Gly Lys Thr Asn
130 135 140	325 330 335
Val Ala Tyr Phe Val Glu Phe Leu Gln Ser Ala Phe Gly Tyr Ser Pro	Asp Val Gly Gln Lys Phe Tyr Leu Asp Thr Gly Asp Ala Ser Asn Phe
145 150 155 160	10 340 345 350
Ser Asn Val His Val Ile Gly His Ser Leu Gly Ala His Ala Ala Gly	Als Arg Trr Arg Tyr Lys Val Ser Val Thr Leu Ser Gly Lys Lys Val
165 · 170 175	355 360 365
Glu Ala Gly Arg Arg Thr Asn Gly Thr 11e Gly Arg 11e Thr Gly Leu	Thr Gly His Ile Leu Val Ser Leu Phe Gly Asn Lys Gly Asn Ser Lys
180 185 190	370 375 380
Asp Pro Ala Glu Pro Cys Phe Gln Gly Thr Pro Glu Leu Val Arg Leu	15 Gln Tyr Glu Ile Phe Lys Gly Thr Leu Lys Pro Asp Ser Thr His Ser
200 205	. 385 390 395 400
Asp Pro Ser Asp Ala Lys Phe Val Asp Val Ile His Thr Asp Gly Ala	Asn Glu Phe Asp Ser Asp Vel Asp Val Gly Asp Leu Gln Met Val Lys
210 215 220	405 410 415
Pro Ile Val Pro Asn Leu Gly Phe Gly Met Ser Gln Val Val Gly His	Phe Ile Trp Tyr Asn Asn Val Ile Asn Pro Thr Leu Pro Arg Val Gly
225 230 235 240	20 420 425 430
Leu Asp Phe Pro Asn Gly Gly Val Glu Met Pro Gly Cys Lys Lys	Ala Ser Lys Ile Ile Val Glu Thr Asn Val Gly Lys Gln Phe Asn Phe
245 250 255	435 440 445
Asn lle Leu Ser Gln lle Val Asp lle Asp Gly Ile Trp Glu Gly Thr	Cys Ser Pro Glu Thr Val Arg Glu Glu Val Leu Thr Leu Thr Pro
260 265 270	450 455 460

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State Stat	.WO 2004/055519 289/335	PCT/EP2003/014057	WO 2004/055519 PCT/EP2003/014057 290/335
462 4210 95 42110 PT 42111 PT 43111 PT 4311 PT 43111 PT 4	Сув		Gln Gly Met Thr Ser Ale Asp Asp Phe Phe Gln Gly Thr Lys Ale
1, 210 95	465		. 56 06 58
4210 552			Leu Ala Gly Gly Thr Thr Met Ile Ile Asp His Val Val Pro Glu
211 572 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272 272			105
115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115 115	<210>		
130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130 130			120
131 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132 132		·	Ser Lys Ser Cys Cys Asp Tyr Ser Leu His Vel Asp Ile Ser Glu
High Dia Gli Gli Gli Wer Gli Ale Eau Val Lya Abp High High Protein 2 131 145 145 150 150 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151 151			135
1322 13 13 13 13 13 13 1	<2220>		His Lys Gly Ile Gln Glu Glu Met Glu Ala Leu Val Lys Asp His C
<pre><222> (1) . (572) <222></pre>		•	145 150 155
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At Ser Tyr Gin Gly Lys Lys Asn IIe Pro Arg IIe Thr Ser Asp Arg 1 20 15 Leu Leu Iie Lys Gly Gly Iys IIe Val Asn Asp Rap Gln Ser Phe Tyr 20 21 22 23 Ala Asp IIe Tyr Met Glu Asp Gly Leu IIe Lys Gln IIe Gly Glu Asn 35 Leu Iie Val Pro Gly Gly Iys Thr Iie Glu Ala His Ser Arg Met 50 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 45 40 40			165
15 10 15 16 15 16 15 16 15 16 15 16 15 16 15 16 15 16 15 16 15 16 16			Thr Asp Cys Gln Ile Tyr Glu Val Leu Ser Val Ile Arg Asp Ile G
1 5 10 And I Leu			185
1 5 10 15 15 15 10 15 15 15 15 15 15 15 15 15 15 15 15 15			
Leu Leu Ile Lys Gly Gly Lys Ile Val Asn Asp Asp Gln Ser Phe Tyr 20 Ala Asp Ile Tyr Met Glu Asp Gly Leu Ile Lys Gln Ile Gly Glu Asn 35 Leu Ile Val Pro Gly Gly Val Lys Thr Ile Glu Ala His Ser Arg Met 50 50 Val Ile Pro Gly Gly Ile Asp Val His Thr Arg Phe Gln Met Pro Asp 65 65	V)	15	200
Ala Asp Ile Tyr Met Glu Asp Gly Leu Ile Lys Gln Ile Gly Glu Asn 35 Leu Ile Val Pro Gly Gly Val Lyg Thr Ile Glu Ala His Ser Arg Met 50 50 Val Ile Pro Gly Gly Ile Asp Val His Thr Arg Phe Gln Met Pro Asp 65 70 75 80	Leu Leu lie Lys Gly Gly Lys lle Val Asn Asp Asp Gln Se	r Phe Tyr	Gin Gin Arg lle Leu Asp Leu Gly Ile Thr Gly Pro Glu Gly His V
Ala Asp Ile Tyr Met Glu Asp Gly Leu Ile Lys Gln Ile Gly Glu Asn 35 40 45 20 Leu Ile Val Pro Gly Gly Val Lys Thr Ile Glu Ala His Ser Arg Met 50 55 60 Val Ile Pro Gly Gly Ile Asp Val His Thr Arg Phe Gln Met Pro Asp 65 77 78 80	20		215
35 40 45 45 45 45 45 45 4	Ala Asp Ile Tyr Met Glu Asp Gly Leu Ile Lys Gln Ile Gl	y Glu Asn	Leu Ser Arg Pro Glu Glu Val Glu Ala Glu Ala Val Asn Arg Ala I
Arg Met Pro Asp 80	35 40	2	225 230 . 235
Pro Asp 80	Leu lle Val Pro Gly Gly Val Lys Thr Ile Glu Ala His Se.	r Arg Met	Thr Ile Ala Asn Gin Thr Asn Cys Pro Leu Tyr Ile Thr Lys Val M
Pro Asp	55		. 250
70 75 80 265	Val ile Pro Gly Gly ile Asp Val His Thr Arg Phe Gln Me		Ser Lys Ser Ser Ala Glu Val Ile Ala Gln Ala Arg Lys Lys Gly T
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1 5	10	15	195 200. 205	
5 Thr Tyr Arg Leu Leu Val Pro Gly Ser Arg His Ile Ser	ly Ser Arg His Ile Ser	Gin Ala Ala	5 Ser Ile Leu Ser Phe Met Gly Ser Phe His Gly Arg Thr Met Gly Cys	Сув
20	25		210 215 220	
Ala Lys Val Asp Val Glu Phe Asp Tyr Asp Gly Pro Leu		Met Lys Thr	Leu Ala Thr Thr His Ser Lys Ala Ile His Lys Ile Asp Ile Pro Ser	Ser
. 35 40	0 45		225 230 .235	240
Glu Val Pro Gly Pro Arg Ser Gln Glu Leu Met Lys Gln		Leu Asn Ile	Phe Asp Try Pro Ile Ala Pro Phe Pro Arg Leu Lys Tyr Pro Leu Glu	Glu
10 50 55	09		10 245 250 255	
Ile Gln Asn Ala Glu Ala Val His Phe Phe Cys Asn Tyr		Glu Glu Ser	Glu Phe Val Lys Glu Asn Gln Gln Glu Ala Gly Cys Leu Glu Glu	Glu
65 70	75	08	260 265 · 270	
Arg Gly Asn Tyr Leu Val Asp Val Asp Gly Asn Arg Met	al Asp Gly Asn Arg Met)	Leu Asp Leu	Val Glu Asp Leu Ile Val Lys Tyr Arg Lys Lys Lys Lys Thr Val Ale	Ala
85	06	95	275 280 285	
15 Tyr Ser Gln Ile Ser Ser Val Pro Ile Gly Tyr Ser Asp		Pro Ala Lieu	15 Gly Ile Ile Val Glu Pro Ile Gln Ser Glu Gly Gly Asp Asn His Ala	Ala
100	105	110	290 295 300	
Val Lys Leu ile Gin Gin Pro Gin Asn Ala Ser Met Phe		Val Asn Arg	Ser Asp Asp Phe Phe Arg Lys Leu Arg Asp Ile Ala Arg Lys His Cys	Сув
115 120	125		310 315	320
Pro Ala Leu Glu Ile Leu Pro Pro Glu Asn Phe Val Glu		Lys Leu Arg	Cys Ala Phe Leu Val Asp Glu Val Gln Thr Gly Gly Gly Cys Thr Gly	Gly
20 130 135	140		20 325 330 335	
Gln Ser Leu Leu Ser Val Ala Pro Lys Gly Met Ser Gln I	o Lys Gly Met Ser Gln L	Jeu Ile Thr	Lys Phe Trp Ala His Glu His Trp Gly Leu Asp Asp Pro Ala Asp Val	Val
145	155		340 345 350	
Met Ala Cys Gly Ser Cys Ser Asn Glu Asn Ala Leu Lys		Thr Ile Phe	Met Thr Phe Ser Lys Lys Met Met Thr Gly Gly Phe Phe Leu Lys Glu	Glu
165	170	175	355 360 365	

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Glu Phe Arg Pro Asn Ala Pro Tyr Arg Ile Phe Asn Thr Trp Leu Gly	<220>
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Val Arg Gly Arg Gly Thr Phe Cys Ser Phe Asp Thr Pro Asp Asp Ser	. Val His Tyr lle Gly Ser Arg Leu Gly Arg Thr Leu Thr Gly Trp Val
10 435 440 445	10 20 25 30
Ile Arg Asn Lys Leu Ile Leu Ile Ala Arg Asn Lys Gly Val Val Leu	Gln Arg Thr Phe Gln Ser Thr Gln Ala Ala Thr Ala Ser Ser Arg Asn
450 455 460	. 35 40 45
Gly Gly Cys Gly Asp Lys Ser Ile Arg Phe Arg Pro Thr Leu Val Phe	Ser Cys Ala Ala Asp Lys Ala Thr Glu Pro Leu Pro Lys Asp Cys
465 470 475 480	. 09 25 09
15 Arg Asp His His Ala His Leu Phe Leu Asn Ile Phe Ser Asp Ile Leu	15 Pro Val Ser Ser Tyr Asn Glu Trp Asp Pro Leu Glu Glu Val 11e Val
485 490 495	65 70 75 80
Ala Asp Phe Lys	Gly Arg Ala Glu Asn Ala Cys Val Pro Pro Phe Thr Ile Glu Val Lys
200	56 06 58
	Ala Asn Thr Tyr Glu Lys Tyr Trp Pro Phe Tyr Gln Lys Gln Gly Gly
20	20 100 105 110
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	WO 2004/055519	PCT/EP2003/014057	WQ 2004/055519 PCTT/RP2)nnt3/ns4/ns
		297/335	298/335
	Asp Pro Ile Asp	Asp Pro Ile Asp Trp Ser Leu Lys Tyr Lys Thr Pro Asp Phe Glu Ser	Ile Ile Thr Pro Pro Thr Pro Ile Ile Pro Asp Asp His Pro Leu Trp
	145	150 155 160	340 345 350
	Thr Gly Leu Tyr	Thr Gly Leu Tyr Ser Ala Met Pro Arg Asp Ile Leu Ile Val Val Gly	Met Ser Ser Lys Trp Leu Ser Met Asn Val Leu Met Leu Asp Glu Lys
		165 170 175	355 . 360 365
٠.	5 Asn Glu Ile Ile	Asn Glu Ile Ile Glu Ala Pro Met Ala Trp Arg Ser Arg Phe Phe Glu	5 Arg Val Met Val Asp Ala Asn Glu Val Pro Ile Gln Lys Met Phe Glu
	180	185 . 190	370 375 380
	Tyr Arg Ala Tyr	Tyr Arg Ala Tyr Arg Ser Ile Ile Lys Asp Tyr Phe His Arg Gly Ala	Lys Leu Gly lle Thr Thr lle Lys Val Asn lle Arg Asn Ala Asn Ser
	195	200 . 205	385 390 395 400
	Lys Trp Thr Thr	Lys Trp Thr Thr Ala Pro Lys Pro Thr Met Ala Asp Glu Leu Tyr Asn	Leu Gly Gly Gly Phe His Cys Trp Thr Cys Asp Val Arg Arg Gly
01	210	215 220	10 405 410 415
	Gln Asp Tyr Pro	Gln Asp Tyr Pro Ile His Ser Val Glu Asp Arg His Lys Leu Ale Ala	Thr Leu Gln Ser Tyr Leu Asp
	225	230 235 240	420
	Gln Gly Lys Phe	Gln Gly Lys Phe Val Thr Thr Glu Phe Glu Pro Cys Phe Asp Ala Ala	
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	1 5 10 15	195 200 205
	Ala Arg Ala Lys Glu Glu Asp Met Gly Thr Val Val Ala Ile His Leu	Lys Arg Glu Gly Glu Lys Asn ile Leu Val Phe Asp Leu Gly Gly Gly
Ñ	20 20 25 30	20 210 215 220
	Gly Thr Thr Tyr Pro Cys Val Gly Val Phe Lys Asn Gly Arg Met Glu	Thr Phe Amp Val Ser Leu Leu Thr Ile Amp Amn Gly Val Phe Lym Val
	35 40 45	225 230 235 240
	ile ile Ala Asn Asp Gln Gly Asn Arg ile Met Pro Ser Tyr Val Ala	Val Ala Thr Aen Gly Asp Thr Tyr Leu Gly Gly Glu Asp Phe Asp Gln
		245 250 255

WO 2004/055519	301/335	PCT/EP2003/014057	WO 2004/055519 302/335	· PCT/EP2003/014057
Arg Val Met Glu His Phe Ile Lys Leu Tyr Lys Lys Lys	Lys Leu Tyr Lys Lys Lys	Thr Gly Lys	Ser Gln Ile Phe Ser Thr Ala Phe Asp Asn Gln Pro Xaa Thr Ile Lys	p.Asn Gln Pro Xaa Thr 11e Lys
260	265	270	450 455	460
Asp Val Arg Lys Asp Asn Arg Ala Val Gln Lys Leu Trp	Ala Val Gln Lys Leu Trp	Arg Lys Val	Val Tyr Glu Gly Lys Gln Pro Leu Thr Lys Asp Asn His Leu Leu Gly	r Lys Asp Asn His Leu Leu Gly
275	280 285		465 470	475 . 480
5 Glu Lys Ala Lys Arg Ala Leu Ser Ser Gln His Gln Ala	Ser Ser Gln His Gln Ala	Xaa Val Ile	5 Thr Phe Asp Leu Thr Gly 11e Pro Pro Ala Pro Cys Gly Val Pro Gln	o Ala Pro Cys Gly Val Pro Gln
290 295	300		485	490.
Glu ile Glu Ser Phe Tyr Glu Gly Glu Asp Phe Ser Glu		Thr Leu Thr	ile Glu Val Thr Phe Glu Met Asp Val Ser Asp Ile Leu Gln Val Thr	l Ser Asp Ilė Leu Gln Val Thr
305 310	315	320 .	500 505	5 510
Gln Ala Lys Phe Glu Glu Leu Asn Xaa Asp Leu Phe Gln		Ser Thr Wet	Ala Lys Asp Lys Gly Thr Arg Tyr Lys Asn Lys Ile Thr Ile Thr Asn	8 Asn Lys Ile Thr Ile Thr Asn
325	330	335	10 515 520	. 525
Lys Pro Ser Gln Arg Ser Val Xaa Lys Val Leu Glu Asp		Ser Asp Leu	Asp Gln Asn His Leu Thr Pro Glu Asp Ile Glu Arg Met Vel Asn Asp	o Ile Glu Arg Met Val Asn Asp
340	345	350	530 535	540
Lys Lys Ser Asp Ile Asp Glu Thr Val Leu Val Gly Gly		Phe Thr Gln	Ala Glu Lys Phe Ala Glu Glu Asp Lys Lys Leu Lys Glu Cys Thr Asp	1 Lys Leu Lys Glu Cys Thr Asp
355	360 365		545	555 560
i lle Pro Lys Ile Gln Gln Leu Val Lys Glu Phe Phe Asn Gly Lys Glu	al Lys Glu Phe Phe Asn		15 Thr Arg Asn Glu Leu Glu Ser Tyr Ala Tyr Ser Leu Lys Asn Gln Ile	i Tyr Ser Leu Lys Asn Gln 11e
376 375	380			570 575
Leu Ser Arg Gly Ile Ser Pro Tyr Glu Ala Val Ala Tyr Gly Ala Ala	fyr Glu Ala Val Ala Tyr (31y Ala Ala	Gly Asp Lys Glu Lys Leu Gly Gly Lys Leu Ser Ser Glu Asp Lys Glu	Leu Ser Glu Asp Lys Glu
385	395	400	580 585	290
Val Gln Ala Gly Val Leu Ser Gly Asp Gln Asp Thr Gly		Asp Leu Val	Thr Met Glu Lys Thr Val Glu Glu Lys Thr Glu Trp Leu Glu Ser His	Thr Glu Trp Leu Glu Ser His
405	410	415	20 595 600	605
Leu Leu Asp 11e Cys Pro Leu Thr Leu Gly 11e Glu Thr	hr Leu Gly Ile Glu Thr V	Val Gly Gly	Gin Asp Ala Asp Thr Glu Asp Phe Lys Ala Lys Lys Lys Glu Leu Glu	Ala Lys Lys Glu Leu Glu
. 420	425 4	430	. 610 615	620
Val Met Thr Lys Leu Ile Pro Arg Asn Thr Val Val Pro Thr Lys Lys	rg Asn Thr Val Val Pro I	thr Lys Lys	Glu ile Val Gin Pro ile ile Ser Lys Leu Tyr Gly Ser Ala Gly Pro	Leu Tyr Gly Ser Ala Gly Pro
435 4	440 . 445		625 630	635 640

303/335	PCT/EP2003/014057	WO 2004/055519 504/335 PCT/EP2003/014057
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645 650		56 06 58
		Arg Thr Cys Gly Phe Asp Phe Gly Gly Asn Ile Ile Wet Phe Ser Thr
		100 105 110
		5 Asp Lys Gln Met Gly Tyr Gln Cys Phe Val Ser Phe Phe Asp Leu Arg
		115 120 125
		Asp Pro Ser Gln Ile Asp Asn Asn Glu Pro Tyr Met Lys Ile Pro Cys
Homo sapiens	• .	130 135 140
		Asn Asp Ser Lys Ile Thr Ser Ala Val Trp Gly Pro Leu Gly Glu Cys
Eukaryotic translation initiation factor 3 subuni	r 3 subunit 2	10 145 150 155 160
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Accession No. as of 29 August 2003: Q13347	347	165 170 175
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		180 185 190
Met Lys Pro lle Leu Leu Gln Gly His Glu Arg Ser lle Thr	: Ile Thr Gln Ile	15 Asp Ile Gln Leu Ser Arg Asp Met Thr Met Phe Val Thr Ala Ser Lys
. 10 .	1.5	195 200 205
Lys Tyr Asn Arg Glu Gly Asp Leu Leu Phe Thr Val Ala Lys	Ala Lys Asp Pro	Asp Asn Thr Ala Lys Leu Phe Asp Ser Thr Thr Leu Glu His Gln Lys
20 25	30	210 215 220
ile Val Asn Val Trp Tyr Ser Val Asn Gly Glu Arg Leu Gly Thr	Leu Gly Thr Tyr	Thr Phe Arg Thr Glu Arg Pro Val Asn Ser Ala Ala Leu Ser Pro Asn
40	45	20 225 230 235 240
Met Gly His Thr Gly Ala Val Trp Cys Val Asp Ala Asp Trp Asp Thr	Asp Trp Asp Thr	Tyr Asp His Val Leu Gly Gly Gly Glu Glu Ala Met Asp Val Thr
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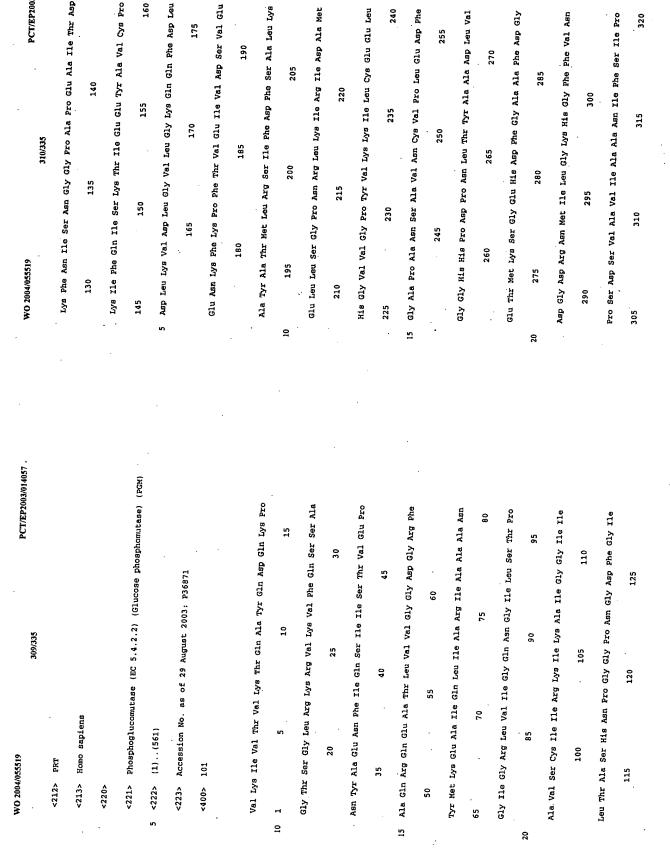
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Asn Ser Val Ala Phe His Pro Asp Gly Lys Ser Tyr Ser Ser Gly Gly	Lys Ser Tyr Ser Ser Gly Gly	Leu lle Val Pro Gly Gly Val Lys Thr Ile Glu Ala His Ser Arg Met
290 295	. 006	
5 Glu Asp Gly Tyr Val Arg Ile His Tyr Phe Asp Pro Gln Tyr Phe Glu		5 Val Ile Pro Gly Gly Ile Asp Val His Thr Arg Phe Gln Met Pro Asp
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Phe Glu Phe Glu Ala		Gln Gly Met Thr Ser Ala Asp Asp Phe Phe Gln Gly Thr Lys Ala Ala
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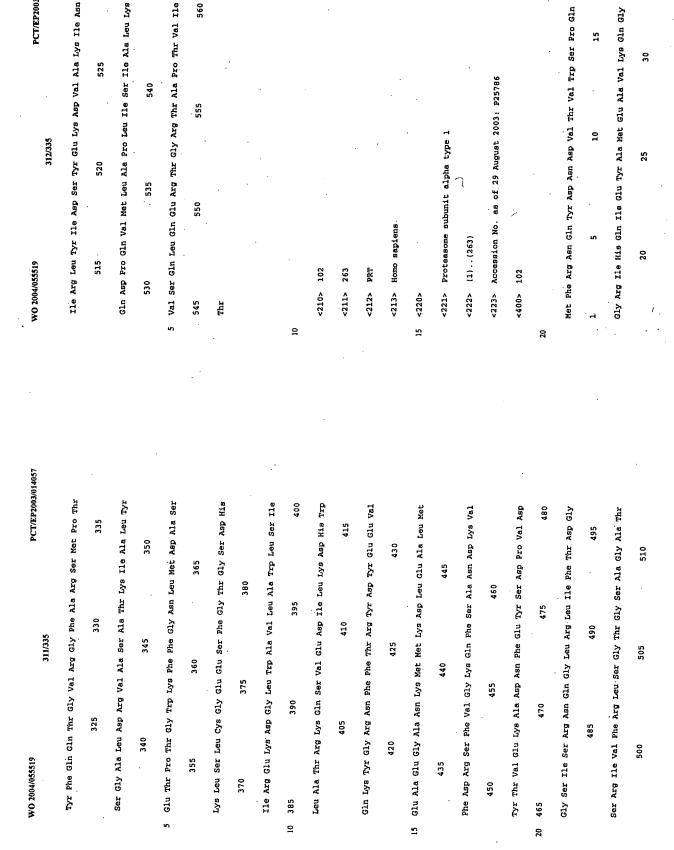
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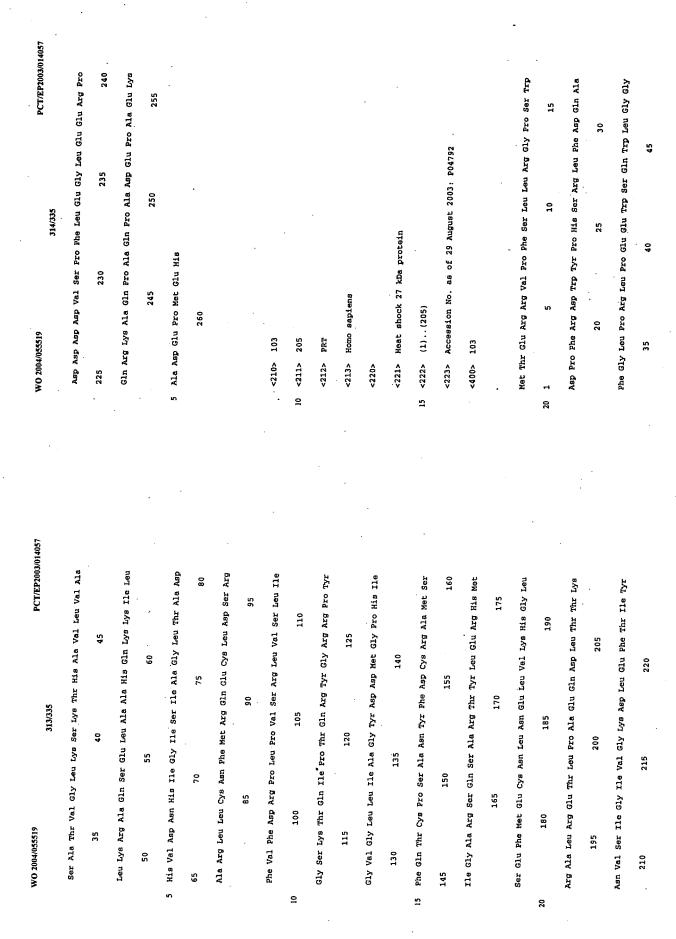
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	245 250 255	435 440 445
	5 Ser Lys Ser Ser Ala Glu Val Ile Ala Gln Ala Arg Lys Lys Gly Thr	5 Gln Gly Lys Ile Val Leu Glu Asp Gly Thr Leu His Val Thr Glu Gly
	260 265 270	450 455 460
	Val Val Tyr Gly Glu Pro Ile Thr Ala Ser Leu Gly Thr Asp Gly Ser	Ser Gly Arg Tyr Ile Pro Arg Lys Pro Phe Pro Asp Phe Val Tyr Lys
	275 . 280 285	465 470 475 480
	His Tyr Trp Ser Lys Asn Trp Ala Lys Ala Ala Ala Phe Val Thr Ser	Arg lle Lys Ala Arg Ser Arg Leu Ala Glu Leu Arg Gly Val Pro Arg
	10 290 295 . 300	10 485 490 495
	Pro Pro Leu Ser Pro Asp Pro Thr Thr Pro Asp Phe Leu Asn Ser Leu	Gly Leu Tyr Asp Gly Pro Val Cys Glu Val Ser Val Thr Pro Lys Thr
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	20 370 375 380	20 565 570
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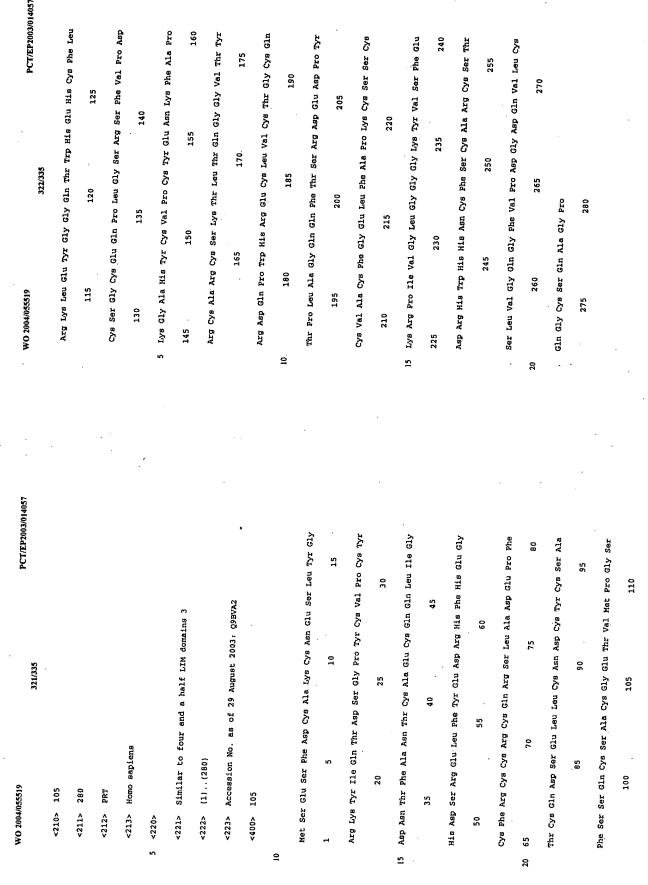
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Asp Glu His Gly	Asp Glu His Gly Tyr Ile Ser Arg Cys Phe Thr Arg Lys Tyr Thr Leu	Lou Ala Lys Pro Leu Val Lys Phe Ile Gln Gln Thr Tyr Pro Ser Gly	. Gly
130	135 . 140	20 25 30	
Pro Pro Gly Val	Pro Pro Gly Val Amp Pro Thr Gln Val Ser Ser Leu Ser Pro Glu	Gly Glu Glu Gln Ala Gln Tyr Cys Arg Ala Ala Glu Glu Leu Ser Lys	LyB
145	150 155 160	35 40 45	
15 Gly Thr Leu Thr	Gly Thr Leu Thr Val Glu Ala Pro Met Pro Lys Leu Ala Thr Gln Ser	15 Leu Arg Arg Ala Ala Val Gly Arg Pro Leu Asp Lys His Glu Gly Ala	Ala
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Asn Glu Ile Thr	Asn Glu ile Thr ile Pro Val Thr Phe Glu Ser Arg Ala Gln Leu Gly	Leu Glu Thr Leu Leu Arg Tyr Tyr Asp Gln Ile Cys Ser Ile Glu Pro	Pro
. 180	185 190	65 70 75 80	80
Gly Pro Glu Ala	Gly Pro Glu Ala Ala Lys Ser Asp Glu Thr Ala Ala Lys	Lys Phe Pro Phe Ser Glu Asn Gln Ile Cys Leu Thr Phe Thr Trp Lys	LyB
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Gly Leu Lys Ile Ala Ala Lys His Tyr Gln Phe Ala Ser Gly Ala Phe	Leu Val Lys Ser Thr Pro Val Asn Vel Pro Ile Ser Gln Lys Phe Thr
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Leu His Ile Lys Glu Thr Val Leu Ser Ala Leu Ser Arg Glu Pro Thr	5 Asp Leu Phe Glu Lys Met Val Pro Val Ser Val Gln Gln Ser Leu Ala
165 170 175	355 360 365
Val Asp Ile Ser Pro Asp Thr Val Gly Thr Leu Ser Leu Ile Met Leu	Ala Tyr Asn Gln Arg Lys Ala Asp Leu Val Asn Arg Ser Ile Ala Gln
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Lys Asp als ile ile als Lys Leu Ala Asn Gln Ala Ala Asp Tyr Phe	Leu Pro Ala Ala Ile Glu Asp Val Ser Gly Asp Thr Val Pro Gln Ser
210 215 220	405 410 415
Gly Asp Ale Phe Lys Gln Cys Gln Tyr Lys Asp Thr Leu Pro Lys Glu	ile Leu Thr Lys Ser Arg Ser Val ile Glu Gln Gly Gly ile Gln Thr
230 235 240	420 425 430
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Glu Tyr His Gln Ser Ile Leu Ala Lys Gln Gln Lys Lys Phe Gly Glu	Glu Ile Leu Asp Glu Ser Leu Arg Leu Leu Asp Glu Glu Glu Ala Thr
260 265 270	450 . 455 460
Glu Ile Ala Arg Leu Gln His Ala Ala Glu Leu Ile Lys Thr Val Ala	Asp Asn Asp Leu Arg Ala Lys Phe Lys Glu Arg Trp Gln Arg Thr Pro
275 280 285	20 465 470 475 480
Ser Arg Tyr Asp Glu Tyr Val Asn Val Lys Asp Phe Ser Asp Lys 11e	Ser Asn Glu Leu Tyr Lys Pro Leu Arg Ala Glu Gly Thr Asn Phe Arg
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Asn Arg Ala Leu Ala Ala Ala Lys Lys Asp Asn Asp Phe Ile Tyr His	Thr Val Leu Asp Lys Ala Val Gin Ala Asp Gly Gin Val Lys Glu Cys
310 315 320	500 505 510

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		320/335
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	Glu Leu Asn Ala Ala Ile Pro Ser Ala Asn Pro Ala Lys Thr Met Gln	Ser lle Pro Thr Pro Ala Tyr Gin Ser Ser Pro Ala Giv Giv He ale
	530 535 540	725 730 736
	5 Gly Ser Glu Val Val Asn Val Leu Lys Ser Leu Leu Ser Asn Leu Asp	Pro Ala Pro Arg Thr Met Pro Bro mhw
	545 550 555 560	740 745
	Glu Val Lys Lys Glu Arg Glu Gly Leu Glu Asn Asp Leu Lys Ser Val	Val Leu Pro Ala
	565 570 575	755 760 765
	Asn Phe Asp Met Thr Ser Lys Phe Leu Thr Ala Leu Ala Gln Asp Gly	Pro Ser Ala Thr Ala Pro Ser Pro Val Gly Ala Gly Thr Ala Ala Pro
H	10 580 585 590	10 770 775 780
	Val 11e Asn Glu Glu Ala Leu Ser Val Thr Glu Leu Asp Arg Val Tyr	Ala Pro Ser Gln Thr Pro Gly Ser Ala Pro Pro Gln ale Cln Ala
	. 509 009 565	785 790 795 PhO
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15	5 Leu Leu Lys Asn Ile Gln Val Ser His Gln Glu Phe Ser Lys Met Lys	Gly Gln Tyr Asn
	625 630 635 640	820 825 830
	Gln Ser Asn Asn Glu Ale Asn Leu Arg Glu Glu Val Leu Lys Asn Leu	Tyr Pro Pro Val Tyr His Gln Ser Pro Gly Gln Ala Pro Tyr Pro Gly
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70	660 665 670	20 850 855 860
	Gly Thr Lys Phe Tyr Asn Glu Leu Thr Glu Ile Leu Val Arg Phe Gln	Tyr Pro Gln Gln
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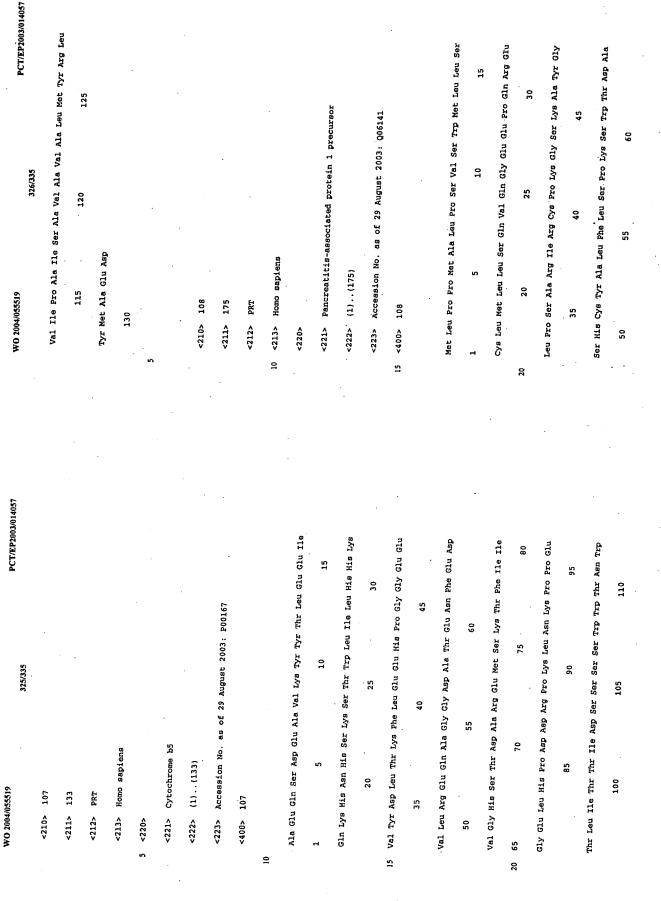


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5 <220>	5 Lys Gly Ala His Tyr Cys Val Pro Cys Tyr Glu Asn Asn Phe Ala Pro
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Arg Lys Tyr 11e Gln Thr Asp Ser Gly Pro Tyr Cys Val Pro Cys Tyr	Cys Val Ala Cys Phe Gly Glu Leu Phe Ala Pro Lys Cys Ser Ser Cys
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. Asp Asn Thr Phe Ala Asn Thr Cys Ala Glu Cys Gln Gln Leu Ile Gly	15 Lys Arg Pro 11e Val Gly Leu Gly Gly Lys Tyr Val Ser Phe Glu
35 40 45	225 230 235 240
His Asp Ser Arg Glu Leu Phe Tyr Glu Asp Arg His Phe His Glu Gly	Asp Arg His Trp His His Aen Cys Phe Thr Cys Asp Arg Cys Ser Aen
09 55 05	245 250 255
Cys Phe Arg Cys Cys Arg Cys Gln Arg Ser Leu Ala Asp Glu Pro Phe	Ser Leu Val Gly Gln Gly Phe Val Pro Asp Gly Asp Gln Val Leu Cys
65 70 75 80	20 260 265 270
Thr Arg Gln Asp Ser Glu Leu Leu Cys Asn Asp Cys Tyr Cys Ser Ala	Gln Gly Cys Ser Gln Ala Gly Pro
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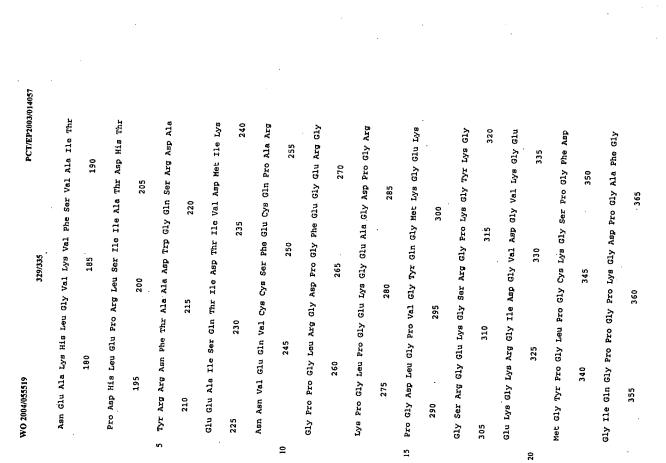
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Gly

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.2

Gly Pro Pro Gly Asp Pro Gly Leu Met Gly Glu Arg Gly Glu Asp Gly

Pro

Pro Ala Gly Asn Gly Thr Glu Gly Phe Pro Gly Phe Pro Gly Tyr

Gly Asn Arg Gly Ala Pro Gly Ile Asn Gly Thr Lys Gly Tyr Pro Gly

Leu Lys Gly Asp Glu Gly Glu Ala Gly Asp Pro Gly Asp Asp Asn Asn

PCT/EP2003/014057

Leu Lys Gly Glu Lys Gly Glu Pro Gly Ala Asp Gly Glu Ala Gly Arg

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Pro Gly Ala Arg Gly Pro Ser Gly Asp Glu Gly Pro Ala Gly Glu Pro

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	-, 511 GIY ALB Thr Pro Ala Ala Ile Glu Lys Ala Val Gln	a ile Glu Lys Ala Val Gin	Met Ser Leu Ser Ale Phe Thr Leu Phe Leu Ala Ten Tie Chan
	945 . 950	955 960	1 5
	Glu Ala Gln Arg Ala Gly Ile Glu Ile Phe Val Val Val Gly Arg	Val Val Val Val Gly Arg	Ser Gly Gln Tvr for her man and man and and and and and and and and and a
	965 970	975	
	5 Gln Val Asn Glu Pro His ile Arg Val Leu Val Thr Gly Lys Thr Ala	Val Thr Gly Lys Thr Ala	5 Ser Ser Ser Dro and Co. 25 30
	980	066	car car Fio Asn Cys Ala Pro
	Glu Tyr Asp Val Pro Tyr Gly Glu Ser His Leu Phe Arg. Val Pro Ser	Leu Phe Arg Val Pro Ser	Say No. 1 and 1 an
	995 1000	1005	met 1yr Cys Asp Glu Leu Lys Leu Lys Ser Val Pro Met Val
	Tyr Gin Ala Leu Leu Arg Gly Val Phe His Cil mu.		50 55 60
10		odin ing Val Ser Arg	Pro Pro Gly 11e Lys Tyr Leu Tyr Leu Arg Asn Asn Gln 11e Asp His
		1020 10	
	Lys Val Ala Leu Gly		Ile Asp Glu for ale phacelle.
	1025		The Ash Val Thr Asp Leu Gln Trp Leu Ile
			85 90
			Leu Asp His Asn Leu Leu Glu Asn Ser Lys Ile Lys Gly Arg Val Phe
15	<210> 110		100 105 110
	<211> 338	51	Ser Lys Leu Lys Gln Leu Lys Lys Leu His Ile Asn His Asn Asn Leu
	<212> PRT		115 120 125
	<213> Homo sapiens		Thr Glu Ser Val Gly Pro Leu Pro Lys Ser Leu Glu Asp Leu Gln Leu
	<2220>		130 135 140
20	<221 - Table 2 -		Thr His Asn Lys 11e Thr Lys Leu Gly Ser Phe Glu Gly Leu Val Acr
i	Tark Decursor	20	145 150 155
	-2447 (1)(338)		Leu Thr Phe Ile His ton on "".
	<223> Accession No. as of 29 August 2003: P51884	P51884	reu Gin His Asn
	<400> 110		175
			Ser Ala Ala Phe Lys Gly Leu Lys Ser Leu Glu Tyr Leu Asp Leu Ser

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Phe Asn Gln Ile Ala Arg Leu Pro Ser Gly Leu Pro Val Ser Leu Leu

Thr Leu Tyr Leu Asp Asn Asn Lys Ile Ser Asn Ile Pro Asp Glu Tyr

5 Phe Lys Arg Phe Asn Ala Leu Gln Tyr Leu Arg Leu Ser His Asn Glu

Leu Ala Asp Ser Gly Ile Pro Gly Asn Ser Phe Asn Val Ser Ser Leu

Val Glu beu Asp beu Ser Tyr Asn Lys Leu Lys Asn 11e Pro Thr Val

Asn Glu Asn Leu Glu Asn Tyr Iyr Leu Glu Val Asn Gln Leu Glu Lys

Phe Asp Ile Lys Ser Phe Cys Lys Ile Leu Gly Pro Leu Ser Tyr Ser

15 Lys Ile Lys His Leu Arg Leu Asp Gly Asn Arg Ile Ser Glu Thr Ser

Leu Pro Pro Asp Met Tyr Glu Cys Leu Arg Val Ala Asn Glu Val Thr

Leu Asn